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FIBROUS DYSPLASIA OF BONE[1]

by

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In the autumn of 1947 the Department of Neurosurgery, State Hospital, Copenhagen, admitted a patient who caused certain diagnostic difficulties, clinical as well as radiological. Her case history will be reported below, and at the same time a few similar cases will be reviewed on the basis of studies of the literature.

Case 1. (Dept. of Neuros. 0554/47.)

A female, aged 25, who had been healthy with the exception of frontal sinusitis 13 years ago. For the last 3 months prior to admission there had been a feeling of fatigue and some nausea, during the last month combined with headache of pressure character, most marked on the right side. The power of concentration was slightly reduced and she had lost weight, 5 kilos, in the course of the months prior to admission. Obj. exam. revealed a protrusion of 2 mm. of the eyeball. No evidence of choked disks, a mild right-sided ptosis, and otherwise no neurologic abnormalities. No abnormal pigmentation. Serum calcium 8.6 mg. per 100 cc., serum phosphorus 4.0 mg. per 100 cc. Basal metabolic rate: 7 per cent, 1 per cent below normal. Roentgen examination of skull (fig. 1): Extensive, not well-defined increased density of the entire right orbital portion of the frontal bone with less marked involvement of the left side. Marked sclerosis of the right ala parva, apparently extending to the ala magna. Some narrowing of the superior orbital fissure. The frontal sinuses as well as the upper right ethmoid cells are filled with bone of irregular structure, and the lower part of the squama frontalis is denser than normal. The middle meningeal artery on the right side is very large. Sella turcica natural. Sutures natural.

Craniotomy was performed on the tentative diagnosis of meningioma en plaque on the right side. The operation revealed a peculiar tumour lying unattached in large preformed bony cavities. The surrounding bone was tender and brittle from invasive growth. Around this part there was again a zone of eburnated firm bony tissue. The tumour encroached upon the frontal sinus and the orbital roof, part of which had to be removed.

Micr. exam.: Tissue from central parts of the tumour-like mass described above: The preparation consists of an irregular mass of connective tissue in places sprinkled with small irregular islets of bony tissue (fig. 2 a & b). The density of the cells in the con-

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Fig. 1. Case I. Increased density of the floor of the anterior cranial fossa with osseous lining and osseous invasion into frontal sinus and ethmoid cell. Dilatation of meningeal arteries.

nective tissue is extremely varied; in the areas holding fewest cells the collagenic fibres are densely and irregularly arranged, in several places with a tendency to whorl formation; in these parts the cells are typical fibroblasts. The richly cellular parts are mainly to be found at the periphery of the specimens and also contain typical fibroblasts, but in addition cells with a more oval or round nucleus, forming a transition to typical osteoblasts to be found close to small irregular islets of non-lamellar bony tissue exhibiting varying degrees of calcification. — Spread in the cellular part there are also multinuclear giant cells, but no typical osteoclasts. The tissue, mainly in the cellular parts, is sprinkled with a number of mostly small, thin-walled blood-vessels. There is no inflammatory reaction and no evidence of malignancy.

Tissue from a bone infiltrated with the tumour-like mass:

The bony tissue is spongy, made up of extremely irregular trabeculae. In the medullary cavities there are only minimal amounts of blood-forming tissue, but several hold fatty tissue. The main part is, however, filled with connective tissue of the not particularly cellular types described above. Along the trabeculae there is in places a border of osteoblasts.

Accordingly the histological diagnosis must be: *Fibrous dysplasia of bone.*

As apparent from the case history it is a question of a disease with rather vague clinical and radiological signs, whereas the histologic picture is characteristic. When the syndrome is borne in mind, one may, however, easily suspect the lesion on the basis of the clinical and roentgen findings, although a definite diagnosis can only be made after histologic examination.

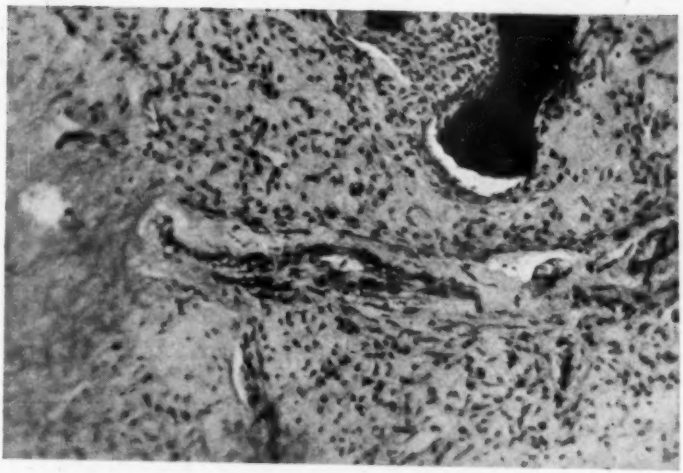

Fig. 2 a. Case I. Connective tissue showing varying density in the arrangement of the cells. One area in a state of degeneration (left-hand corner). Around the bony tissue transition to cells resembling osteoblasts. (× 135). H. E.

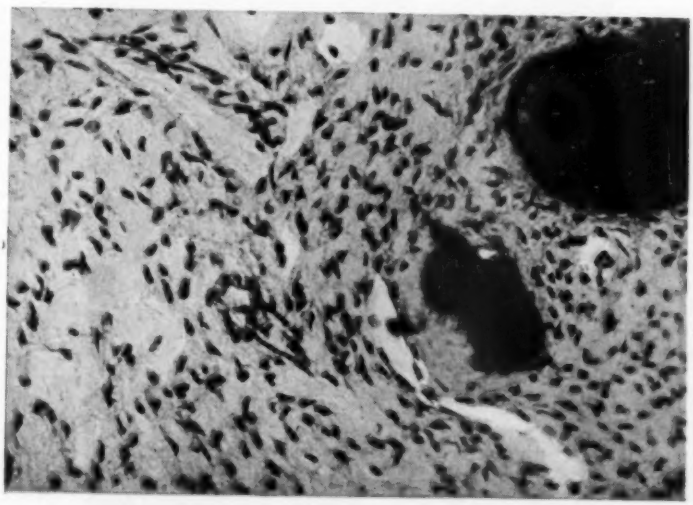

Fig. 2 b. Part of Fig. 1. (× 270).

Fig. 3. Case II. Increased density of the floor of the anterior cranial fossa with osseous lining and partial invasion into the ethmoid cells.

Fig. 4. Case II. Antero-posterior view showing the cyst-like translucency in the osseous lining.

The following case history will serve to illustrate this further:

Case 2. A male, aged 35, was admitted to the State Hospital, Department of Neurosurgery (01043/48) a few months after the first patient, after having been radiographed at the Copenhagen County Hospital in Gentofte.

There was a history of an osseous tumour above the right eye which had been growing slowly for the last 20 years and which gradually displaced the eye. For this reason operation had been performed at the State Hospital Department C 15 years ago involving removal of that part of the growth which was in the frontal sinus. The tumour had only grown slightly since then. During the last few years prior to admission to the Dept. of Neurosurgery, there had been symptoms resembling absences and some atypical déjà-vue phenomena. Now and then mild headache. — Obj. exam.: In the right superciliary ridge there is a groove-like depression and below that an osseous swelling. Displacement of the eyeball 7 mm. downwards and 3 mm. forwards. Neurological nothing abnormal. No abnormal pigmentation.

Roentgen examination of skull (fig. 3 & 4): Increased density, 2—3 cm., of the right portion of the frontal bone with a central area of translucency where the structure is wiped out and mottled. The sclerosing involved the right ala parva, whereas the frontal sinuses appeared to be unaffected. Vessels, sutures, and sella turcica natural. Radiography of all other bones failed to reveal roentgen changes.

Bearing the previous case in mind the microscopic specimen made in the State Hospital, Department C in 1934 was revised.[1] At that time there had been some doubt as to the histological diagnosis. After the syndrome of fibrous dysplasia of bone has been described in such detail in the literature, it was now clear that it must be a question of this lesion.

Craniotomy removing a bony cyst, somewhat larger than a walnut, whose walls contained several peculiar pieces of bone resembling sequestra. After the excision the entire orbital roof had been removed.

Micr. exam.: The wall of the bony cyst was made up of spongy bony tissue with preserved lamellae almost everywhere, whereas there were comparatively few osteocytes in the tissue (fig. 5). In the cavities of the bony tissue, which varied considerably in size, there was hardly any blood-forming tissue, but some loose connective tissue with a few thin-walled blood vessels. No osteoblasts or osteoclasts were seen in this piece.

Tissue resembling sequester from the wall of the cyst contained a few large and several small pieces of bone whose structure was on the whole obliterated, showing neither lamellae nor osteocytes. Particularly between the small pieces of bone there was a rather cellular connective tissue with comparatively few blood vessels. The appearance of the cells varied from spindle shape to more rounded forms. They were disposed in irregular strands. Actual osteoblasts were not demonstrable in this piece of tissue and neither were giant cells.

Tender, greyish red *tissue from the periphery of the cyst* proved to consist of irregular spongy bony tissue with rather dense cellular connective tissue in its cavities. The bony tissue held some osteocytes, but the lamellar pattern was mainly lost. The degree of calcification was greatly varied. Where the bone merged with the connective tissue there was in several places a border of typical osteoblasts. In the immediate vicinity of the latter the connective tissue exhibited a number of rounded cells forming a transition to longish fibroblasts. No giant cells, moderate vascularity.

The *remainder of the contents of the cyst* consisted of a rather acellular and avascular connective tissue arranged in irregular strands, often with a tendency to whorl formation.

[1] Our thanks are due to Professor E. DAHL-IVERSEN, M. D. for the permission to use Dept. C's preparations.

In several places there was a certain homogeneization, but there was not actual hyaline degeneration. Most of the cells were longish with a rod-shaped nucleus; yet a few cells were more stellate in appearance. There was no evidence of inflammation.

In this case too the histologic appearance was typical of fibrous dysplasia of bone.

A search of the case records of the Department of Neurosurgery brought still another case to light:

Case 3. (Dept. of Neuros. 815/37.) A female, aged 26, who for the last 3 years had been noticing a diffuse swelling in the left side of the forehead, suddenly increasing 1 year prior to the admission to the Department of Neurosurgery. There was a history of constant left-sided headache and during the last 6 months a few attacks of dizziness when the headache was worst. *Obj. exam.* revealed diffuse swelling of the left frontal bone with a firm tumour, about the size of a hen's egg, of the frontosphenoidal process and the portion temporal to the latter. Downwards displacement of the left eyeball and some exophthalmos. Otherwise no neurol. abnormalities.

Roentgen examination showed hyperostosis of the lower part of the left frontal bone including the orbital roof and the adjoining part of the left temporal bone. Pelvis, hip joints and hands failed to show anything abnormal.

Operation, employing Dandy's incision, revealed a swelling, as large as a tangerine, consisting of tender greyish red bony tissue without signs of actual neoplasm. There could be no question of removing all the morbid tissue, as it would have entailed a monstrous facial deformity.

Micr. exam. in 1937: The tissue does not appear to be malignant. It is more like a fibrous, chronic form of osteitis fibrosa, as it seems warrantable to rule out Paget's osteitis deformans and osteoma.

Revision of the preparation in 1948 (ERNA CHRISTENSEN)*:* The specimen of bone proves to be made up of strands of cellular bony tissue interrupted by fibroblastic tissue or by cellular connective tissue, completely filling up medullary cavities and surrounding the blood vessels. There are no osteoclasts, but in several places osteoblasts at the edges of the bony strands.

Histol. diagn.: Fibrous dysplasia of bone.

A search of the material from the Roentgen Department of the Copenhagen County Hospital in Gentofte also revealed a case of this condition. Unlike those mentioned above it was localized to the limbs.

Case 4. Copenhagen County Hospital, Dept. D, Case rec. 1737/45. A male, aged 61. During the last 5 years now and then sharp pain in the right elbow. Six weeks prior to admission he suddenly got severe pain in the elbow while working in the garden.

Roentgen examination revealed changes in the entire proximal half of the right ulna consisting of partly well-defined, longish, cyst-like areas of translucency showing expansion of the narrowed cortex. Between these translucent spaces there were spread strands of sclerotic bony tissue. No periosteal reaction. The humero-ulnar joint space was normal. A fracture line through the root of the olecranon process without dislocation.

As there was a history of urinary gravel urography was performed. This led to the discovery of a rather well-defined translucency, about the size of a nut kernel, in the conjoined rami on the right side. It was surrounded by a bony tissue with a spongy substance of a coarse-meshed pattern, poor in calcium.

Ambulant radiography (fig. 6) about 6 months after the admission showed healing of the ulnar fracture, but otherwise unchanged conditions.

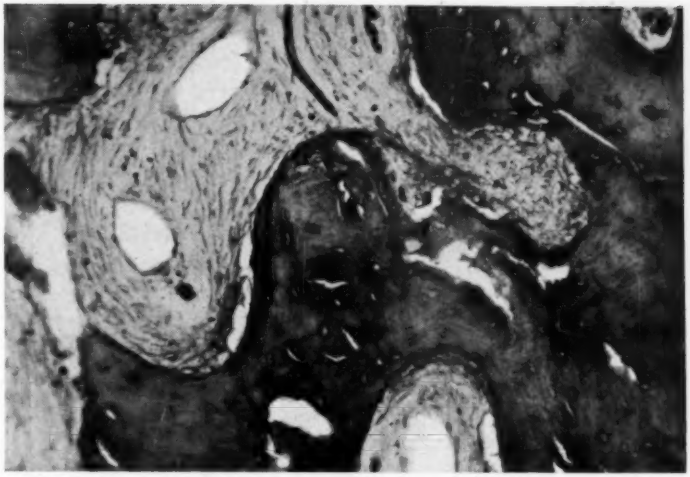

Fig. 5. Case II. Bony tissue. The lamellar disposition is lost and there is loose connective tissue in the medullary cavity. Large, thin-walled vessels in the connective tissue (× 135). H. E.

During the stay at Department D a biopsy specimen showed:

»After decalcification of the large pieces of bone quite thin or slightly thicker spongy bone strands may be seen, usually densely placed. Surrounding the strands there are osteoblasts or in places, arranged in small lacunae, osteoclasts. The bone marrow is somewhat vascularized, hyperemic, consisting of several fine fibrils and in places infiltrated with lymphocytes. It does not exhibit any atypical epithelial cells or any signs of sarcomatous changes. In a few areas the osteolytic processes are quite marked and are vaguely reminiscent of osteitis fibrosa.»

Hist. diagn.: Spongy bone, showing in places changes reminding of osteitis fibrosa. Revision of the preparation shows that it is a case of fibrous dysplasia (sd. Søeborg-Ohlsen).

It is a characteristic feature of this case history that the fibrous dysplasia was not ascertained until it had caused a pathological fracture. At times the lesion does not give any manifestations which can lead one to suspect it after clinical examination, and it is then only discovered at autopsy. The last case history affords an example.

Case 5. (Inst. of Forensic Medicine, P. M. 9/46.)[1]

A female, aged 59, receiver of invalid pension. The patient died after an injury to the skull. Her data in connection with the invalid pension do not state anything about subjective or objective signs of cranial symptoms. (There was no roentgen record of the skull.)

[1] We are indebted to Professor K. Sand, M. D. for the permission to publish this case and to H. Gormsen, M. D. for having called our attention to it.

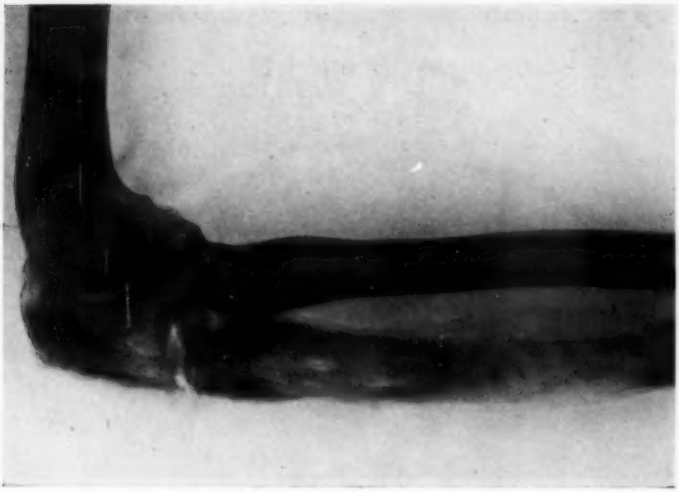

Fig. 6. Case IV. Right ulna: Irregular, cyst-like areas of translucency in the shaft; thin expanded cortex. No periosteal reaction. Pathological fracture.

The patient received the invalid pension on account of arthrosis of the left hip. Roentgen examination of the pelvis showed a vaguely demarcated area of rarefaction with coarse-meshed spongy substance on the left side of the sacral bone. The right side was natural.

Post-mortem examination: Marked thickening of the cranial bones, particularly of the frontal bone which was up to 14 mm. in thickness. On the inside of the calvarium there were small bony plates jutting out into the cranial cavity. There were no irregular bony outgrowths as seen in hyperostosis ossis frontalis. All the bones of the calvarium were extremely tender, and beneath the thin inner and outer bony lamellae there was a proliferative spongy tissue which was very soft and imbibed with blood which gave it a peculiar bluish tinge. In addition to the frontal bone the changes also involved the parietal bones and the base of the skull and occipital bone. Moreover, there was less marked involvement of the central portion of the ethmoid bone and both orbital roofs which also exhibited a number of fissures, especially on the left side. A large epidural hematoma was found behind the frontal bone on the right side and a smaller one in the corresponding site on the left.

Micr. exam. revealed: Cranial bones: All showing the same changes: Spongy bony tissue, the medullary cavities filled with fibrous tissue with fine fibrils containing sparse to moderate amounts of marrow cells. Between the bony and fibrous tissue there was every-where a single row of osteoblasts. Extensive fresh hemorrhages in the tissue. No evidence of sarcoma. The tissue did not remind of osteoid tissue. Hist. diagn.: Fibrous dysplasia of bone (sd. HARALD GORMSEN).

The lesion represented by the case histories reported above affords a rather heterogeneous syndrome, the most prominent symptom of which is a proliferative connective-tissue process in one or more bones. Frequently the bony lesion is the only symptom. This was so in all our cases.

In instances where the osseous process involves numerous bones, there may also be an abnormal pigmentation of the skin and, in females, precocious puberty. Individuals of both sexes may, in addition, exhibit early onset and early arrest of bone growth. — As in other diseases involving an abnormal breakdown of bone, advanced cases of fibrous dysplasia usually display an increased content of phosphatase in the blood serum. Other pathologic changes have not been ascertained in the blood.

As regards the course of the disease, it is typical for the processes to maintain their extent at the time when bone growth is arrested. As in one of our cases the lesion sometimes escapes discovery until at an advanced age, and then usually only because it has given rise to pathological fractures. In a few instances the lesion is only discovered on the autopsy table as seen from the last case history.

WEIL (1922) appears to have been the first to describe a case of this kind. He interpreted the disease as »eine ungewöhnliche Form der Osteopsathyrose». In 1937 MCCUNE & BRUCH gave a detailed description of a case met with in a 9-year-old girl, reviewing, at the same time, a number of cases from the literature. These authors are, however, greatly in doubt about its nature. The classic description of the disease is, however, usually considered to be a paper by ALBRIGHT et al. (1937), for which reason the disease has also been given the name: Albright's syndrome. This paper sets out the main symptoms and at the same time calls attention to the tendency of the disease to unilateral involvement and to progression. On the basis of the histological findings it is proposed to term the disease: Osteitis fibrosa localisata disseminata. In a later publication (1947) ALBRIGHT dissociates himself from this name as well as from the term Albright's syndrome. Instead he inclines to the term proposed by LICHTENSTEIN (1938): polyostotic fibrous dysplasia. In view of the fact that the lesion often is monostotic, LICHTENSTEIN & JAFFE (1942) changed the name to »fibrous dysplasia of bone», a term which now is gaining ground, although it may rightly be objected that it does not pay regard to the frequent presence of extraskeletal symptoms. In 1942 LICHTENSTEIN & JAFFE collected all the cases known so far, adding 23 of their own, which makes 90. Lastly, SCHLUMBERGER (1946) studied 69 cases at the Army Institute of Pathology during World War II; of them 67 were monostotic.

Opinions are extremely divided on the *etiology* of the disease. POMMER (1920) is of opinion that intra-osseous hemorrhages may cause the fibrous tissue in the bone marrow, perhaps with secondary formation of cysts. ADAMS et al. (1940), however, state that the lesion has never been encountered in hemophiliacs.

A somewhat similar etiology has been ventilated by FURST & SHAPIRO (1943) who compare fibrous dysplasia to Ollier's disease. These authors mention experiments made by P. G. K. BENTZON (1924) who succeeded in producing changes reminding of Ollier's disease in rabbit bones, partly following destruction of one sympathetic trunk by paravertebral injections of alcohol, partly by means of alcohol injections around the tibial nutritive canals. In the light of his experiments BENTZON concluded that a reduction of the sympathicotonia on one side of the body should give rise to bony hyperemia which should be the cause of the changes. It is true that this sympathicoschisis is in conformity with the predominance of unilateral involvement in both diseases, but as far as fibrous dysplasia is concerned, it does not afford a satisfactory explanation of the extraskeletal changes.

The possibility of embryonal disturbances, not further specified, is mentioned by LICHTENSTEIN (1938), FURST & SHAPIRO (1943) and DOCKERTY et al. (1945).

The possible significance of trauma is emphasized by SCHLUMBERGER (1946) whose large material (67 monostotic) contained 3 cases in which he considered local injury to have caused bony changes in the ribs. In both cases reported by FURST & SHAPIRO (1943) there was a history of cranial trauma in early childhood, before the symptoms were observed.

Finally, it should be mentioned that fibrous dysplasia has been seen to coincide with jaundice of the newborn (FURST & SHAPIRO 1943) and with encephalitis (DOCKERTY et al., 1945).

Accordingly, the same applies to fibrous dysplasia as to several other lesions with a low mortality: it is difficult to get to the bottom of the problem of etiology. The writers' cases do not either afford a hint in any definite direction. Actually, one cannot now offer more concrete facts with regard to the etiology than ALBRIGHT et al. did in their original paper from 1937 which called attention to developmental, perhaps nervous disturbances as the most probable cause of the lesion.

Roentgen Appearances

The site of predilection appears to be the long bones of the lower limbs, but the lesion has been met with in all bones. The roentgen manifestations are usually central (though sometimes subperiosteal (DOCKERTY et al., 1945)) cyst-like areas of translucency, usually vaguely defined, and as a rule containing rather coarse trabeculae.

In most cases the changes are found in the metaphysis or in the middle of the bone. If they do involve the epiphysis the joint surface is spared (JAFFE, 1945). The process may erode the cortex from within, the latter expanding and getting thinner than normal. On the inside a wavy erosion

will be seen. The cortex is not broken. There are no periosteal changes except in connection with fractures.

Localized zones of sclerotic bone may be found in between the osteoporotic areas. The sclerosis may even dominate (*e. g.* in the anterior part of the base of the skull and in the maxilla). In between the affected bones the structure is normal.

The bones may grow more rapidly than normal and thus attain an abnormal length. On the other hand there is often premature epiphyseal closure, with resulting shortening. Deformities are not infrequently observed, particularly bowing of the long bones.

The changes affecting the calvarium, the occipital bone and the mandible do not differ from what has been described above. In the anterior part of the base of the skull and in the maxilla, however, the disease is of a special character, manifesting itself in the form of proliferation of dense bone (sometimes with central cyst-like rarefied areas), gradually filling up the accessory nasal sinuses and often causing a thickening of the orbital roof which in turn results in protrusion of the eyeball. The cranial changes are also unilateral and therefore give rise to facial asymmetry. There may be ample vascularization, also unilateral as a rule.

An extremely detailed description of the special cranial changes and their relation to the condition known as leontiasis ossea has been given by WINDHOLZ (1947).

Differential Roentgen Diagnosis

When faced with the radiogram the differential diagnoses are numerous. The most important characteristics of the diseases with which fibrous dysplasia of bone may be confused will be briefly stated below. (In this connection the extra-skeletal changes of fibrous dysplasia will be left out of account.)

Osteitis fibrosa, Recklinghausen's disease, shows, apart from the cyst-like areas, ordinary osteoporosis. The calcium and phosphorus metabolism is generally affected. The age of predilection is stated to be 20 to 50 years.

Giant cell tumour cannot be differentiated with any certainty from fibrous dysplasia on the radiogram. This too is usually of juxtaepiphyseal localization, showing expansion of a thin cortex around a clear area traversed by trabeculae. The most common age is stated to be 20 to 40 years.

Lipiodoses — particularly Hand-Schüller-Christian's disease — may also be confused with fibrous dysplasia. The most common site is the skull and the pelvis, whereas the long bones are seldom involved. The

bony defects are usually well-defined, »map-like», but it is especially the cranial localization which may give rise to symptoms of a nature similar to those of fibrous dysplasia in the orbital roof. The disease usually occurs in early life.

Paget's disease (osteitis deformans) which may be monostotic as well as polyostotic, may — especially in the skull — be indistinguishable from fibrous dysplasia. When occurring in the long bones and the bones of the trunk, Paget's disease may also afford certain difficulties, especially when it is attended with breakdown of bony tissue. The most common age for this condition to occur is 60—70 years. The unilateral involvement of polyostotic fibrous dysplasia may give a diagnostic hint.

Multiple chondromas, Ollier's disease, is also in most cases unilateral. Often it manifests itself by gross changes in the long bones of the hands and feet (in 4 of ALBRIGHT's cases of fibrous dysplasia these bones were also involved, but only mildly and without the characteristic deformity attending Ollier's disease). Epiphyses are preferred to metaphyses (DOCKERTY et al., 1945). The long translucent stripes in the bones, characteristic of Ollier's disease, have also been seen in fibrous dysplasia. The same applies to the wavy erosion on the inside of the cortex.

The solitary chondroma, in its severe forms in hands and feet, also gives rise to vast gross changes, but in mild cases it may closely resemble fibrous dysplasia.

Osteoma of the skull which is well-defined with rounded contours and a dense homogeneous structure can hardly be confused with fibrous dysplasia.

Certain forms of *osteomyelitis*, on the other hand, may resemble monostotic fibrous dysplasia, particularly the subchronic bony abscesses without periosteal reaction, especially when they end in fibrosis.

Metastatic carcinoma of bone, of the ordinary osteolytic type as well as of the osteoblastic type, may remind of fibrous dysplasia. In such cases a knowledge of the primary tumour will help in the diagnosis which is particularly difficult in cases of metastatic deposits in or from the accessory nasal sinuses and the nasopharynx.

Osteogenic sarcoma, which is polymorphous, may in several cases be impossible to distinguish from fibrous dysplasia on the basis of the roentgen appearances alone. Most varieties are, however, rapidly growing (except fibrosarcoma) and break through the cortex. The formation of spicules also helps to differentiate it from fibrous dysplasia.

As regards *Ewing's tumour*, it will hardly cause any difficulties of differential diagnosis because of the periosteal reaction.

Osseous changes in *Hodgkin's disease* may be of a roentgen appearance reminding of fibrous dysplasia because of the polymorphous picture of destruction and proliferation — often in the same bone.

Solitary bone cyst may also be indistinguishable from fibrous dysplasia on the roentgen film.

As far as the cranial lesions are concerned the main difficulty of differentiation will be from *meningioma in the anterior cranial fossa*, as the roentgen appearance and clinical signs of this condition may remind closely of fibrous dysplasia. Still, meningioma will probably not give a picture of cystic areas of translucency, as in our case No. 2. In our patient No. 1 the syndrome was indistinguishable from a meningioma en plaque, as she even showed the same ample vascularization which is typical of meningioma. According to WINDHOLZ (1947) the changes resulting from meningioma begin in the inner table, whereas fibrous dysplasia first causes changes in the diploë. It is, however, doubtful whether this limit can be drawn definitely on the roentgen film. The writers do not agree with TORKILDSEN (1948) who maintains that roentgen examination gives a definite diagnosis of meningioma en plaque.

Differential diagnoses to be considered in everyday practical work when the roentgen appearances are to be interpreted on the basis of the clinical findings before a biopsy specimen has been obtained, are therefore particularly osteitis fibrosa (Recklinghausen's disease), giant cell tumour, solitary chondroma, solitary bone cyst, and, as far as the cranial changes are concerned, meningioma en plaque.

It is evident from what has been said above that the condition is clinically extremely heterogeneous and that in numerous cases the roentgen findings are rather uncharacteristic. This does not, however, apply to the pathological picture which always is typical, and therefore the diagnosis can be made by means of biopsy in cases of doubt. The writers' cases have only given occasion to study the structure of the osseous changes, and therefore the following report of the pathological findings only applies to them. The available literature deals almost exclusively with the skeletal changes.

Pathology

If the lesion has its site in a bone of the extremities, it as a rule will produce a fusiform or oval swelling. Here the bony tissue as a rule is made up of a quite thin shell, smooth on the outer surface and without any periosteal reaction, unless it has been a question of pathological fracture. The endosteal surface, on the other hand, is irregular with thin trabeculae or remains of trabeculae extending into the proliferative connective tissue which fills the medullary cavity completely at this site. In most cases the connective tissue is of a yellowish white colour and of a rather firm, often rubbery consistency. At times the tissue exhibits several large or small cyst-like cavities filled with an amber fluid. More-

over there will be hemorrhages of varying extent. There is a quite sharp limit against the adjoining normal bony tissue. — In the other bones the process has a corresponding appearance. Of this the cases reported in the present paper are good examples.

As regards the microscopic picture, the writers' cases are also typical. Briefly, it may be stated that the microscopic appearance is dominated by a substitution of the medullary tissue by connective tissue. The density of cells and fibrils varies. Often it is arranged in interlacing bundles and whorls; there is usually ample vascularization. Especially in the peripheral areas the tissue is sprinkled with trabeculae of new, non-lamellar, partly calcified bony tissue, presumably formed by metaplasia of connective tissue, transitional forms being demonstrable of connective-tissue cells to osteocytes (SCHLUMBERGER, 1946). There are no or only occasional osteoclasts, but osteoblasts are fairly often observed. Around the vessels there are in a few cases foam cells, but they are exceptional as are also small islets of cartilage. At times there may be small groups of basophile, multi-nuclear giant cells in the fibroid tissue (FURST & SHAPIRO, 1943).

Otherwise the structure varies somewhat in the different parts of the tissue. In the areas showing particularly marked radio-transparency connective tissue dominates. The latter may vary in appearance, ranging from fibroma-like tissue to tissue in a state of degeneration, holding cystic cavities of varying size and shape with slightly eosinophile, granulated contents. — In radiopaque areas there is a more or less calcified, partly newly formed bony tissue. The appearance reminds of inflammatory processes where non-lamellar bony tissue is formed on the surface of a normal lamellar tissue. Ossification is most pronounced where the mechanical action is greatest, as *e. g.* in the anterior part of the base of the skull (WINDHOLZ, 1947). As apparent from the description of the roentgen findings, this site occupies an exceptional position also with respect to the roentgen appearance.

As regards the *histological differential diagnosis*, it did not give rise to much discussion in our cases.

Fibrous dysplasia is distinguishable from *osteitis fibrosa generalisata* (Recklinghausen's disease) in exhibiting few or no osteoclasts.

According to SCHLUMBERGER (1946) differential diagnosis is mainly from *ossifying fibroma* and *non-osteogenic fibroma*. He does not, however, attach much importance to an exact distinction being made, as there may in his opinion be an even transition from fibrous dysplasia to the conditions mentioned.

Differentiation of fibrous dysplasia from *neurofibromatosis* has been subject to most discussion. On the basis of their common features, THANNHAUSER (1944) maintained that the two lesions were identical. He has,

however, been vigorously opposed by JAFFE (1945), ALBRIGHT (1947), and SCHLUMBERGER (1946) who stress the fact that unlike neurofibromatosis, fibrous dysplasia has never been known to exhibit nerve fibres in the tissue.

DOCKERTY et al. (1945) have observed a case which could have been confused with *giant cell tumour*, whereas SNAPPER et al. (1933) have reported an unquestionable case of fibrous dysplasia where foam cells predominated to such an extent that they considered the possibility of xanthomatosis. It is, however, extremely rare that giant cells or foam cells occur in numbers sufficient to obscure the histological picture (cf. ALBRIGHT, 1947).

Treatment

As regards treatment, it is a matter of course that a causal therapy cannot be indicated in view of the doubtful etiology. The treatment may consist, as in 3 of the writers' cases of cranial involvement, in surgical removal of the pathological tissue, if the lesion gives rise to cerebral symptoms. In a few cases where the lesion has been localized to the limbs, the treatment has been removal of the pathological tissue and implantation of bone grafts into the excochleated cavity. Pathological fractures are stated to heal satisfactorily, but to have a tendency to recur (DENSTAD, 1940).

SUMMARY

Fibrous dysplasia of bone is a condition primarily characterized by a proliferative connective-tissue process in the medullary cavity of the bones, affecting one or more bones. Extensive bony involvement may often be unilateral and frequently combined with areas of abnormal pigmentation of the skin, early onset and early arrest of bone growth and — in females — precocious puberty. It has a benign course. It may be impossible to make a diagnosis on the basis of the roentgen findings, whereas the histological picture is well-defined. The etiology is doubtful. The writers report five cases of their own.

ZUSAMMENFASSUNG

Fibröse Knochendysplasie ist ein Zustand, für den in erster Linie ein einen oder mehrere Knochen angreifender, proliferativer Bindegewebsprozess in der Markhöhle der Knochen charakteristisch ist. Ausgedehnte Knochenerkrankung kommt oft einseitig vor und ist häufig mit fleckenwesier abnormer Hautpigmentierung, frühem Beginn und frühem Aufhören des Knochenwachstums sowie — beim weiblichen Geschlecht — mit vorzeitiger Geschlechtsreife kombiniert. Die Krankheit zeigt gutartigen Verlauf. Es kann unmöglich sein, an Hand des Röntgenbefundes die Diagnose zu stellen, während das histologische Bild charakteristisch ist. Die Ätiologie ist zweifelhaft. Verff. berichten über fünf eigene Fälle.

RÉSUMÉ

La dysplasie fibreuse de l'os est une affection caractérisée en première ligne par un processus prolifératif portant sur le tissu conjonctif de la cavité médullaire et atteignant un ou plusieurs os. Un envahissement étendu du squelette peut souvent rester unilatéral, et fréquemment se combiner avec des plages de pigmentation anormale de la peau, un début et un arrêt prématurés de la croissance osseuse et — chez la femme — une puberté précoce. L'évolution de l'affection est bénigne. Il peut être impossible d'en poser le diagnostic en se basant sur les constatations radiologiques, tandis que l'image histologique est bien définie. L'étiologie en est douteuse. Les auteurs rapportent cinq cas qui leur sont personnels.

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FROM THE RADIOPATHOLOGICAL INSTITUTE (CHIEF: PROF. O. REUTERWALL) AND THE GENERAL DEPARTMENT OF RADIUMHEMMET (CHIEF: PROF. E. BERVEN), STOCKHOLM, SWEDEN

TUBERCLE-LIKE STRUCTURES IN LATE IRRADIATION INJURIES OF THE SKIN[1]

by

Lars-Gunnar Larsson

The histology of the late skin changes after roentgen or radium treatment was already described in the beginning of this century (UNNA, GASSMANN, DARIER, ELLIS, WOHLBACH a. o.) and little has since been added. Following the irradiation, degenerative, exudative and reparative changes appear which gradually result in the rather characteristic late picture. The degree of these alterations depends upon the dosage of the treatment, the time elapsed, and the properties of the treated skin. Exogenous factors after the treatment (sunlight, trauma and infection) also play a rôle, such as in causing necrosis.

In the corium and the subcutis we find dense, hyaline collagenous connective tissue, poor in cells, sometimes with fibrinoid degeneration; changes in the elastic fibres are also described. Some of the blood vessels show obliterative changes (hyaline degeneration of the walls and thromboses) and teleangiectases can be noted in the corium. Necrotic areas sometimes appear, probably as a result of the obliterative changes in the blood vessels and often elicited by the above mentioned exogenous factors. Parallel changes are seen in the epidermis with atrophy of its appendages, ulceration and hyperplasia.

Beside these well-known changes, REUTERWALL and co-workers at the Radiopathological Institute have often observed tubercle-like structures with epithelioid and giant cells in previously irradiated skin. These structures closely resemble the granulation tissue in tuberculosis. Because clinical signs of a specific skin disease have not been found and because advanced irradiation changes of the usual type have always been present as well, these tubercle-like structures have been regarded as sequelae of the irradiation. Tubercle bacilli have not been demonstrated in the sections. In almost all cases these changes have appeared after implantation of radium needles.

[1] Submitted for publication, Nov. 25, 1948.

Table 1

Summary of 26 cases with tubercle-like changes in late irradiation injuries of the skin

Case No.	Record No.	Primary Tumour and Irradiation Treatment In all cases, except case 13 and case 23, radium needles were used, containing 10 mg Ra element and with a filter equivalent of 0.9 mm lead; active length 8 mm, diameter 2.3 mm. The distance between the needle axis was usually 4—5 mm.	Time elapsed after first irradiation		Clinical findings		Biopsy	Excision	Microscop. findings			
			Years	Months	Ulcer	Nodules			Recurrence	Degen. connective tissue	Necrosis	Tubercle-like changes
1	7408/37	Basal-cell carcinoma (bc), skin of lip. Implantation: 10 needles, 3½ hours.	3		+		+			+	+	+
			3	6		+	+			+	+	+
2	2928/35	Recurrence of an operated bc behind left ear. Implantation: 12 n., 4 h.	6	2	+	+	+			+		
			6	4	+			+		+	+	+
3	4220/35	Bc, cheek. Implantation: 6 n., 4 h.	7	1	+			+		+	+	+
4	1414/38	Bc, cheek. Implantation: 6 n., 4 h.	4	5	+			+		+	+	+
5	3609/36	Basi-squamous carcinoma, nose. Implantation: 4 n., 4 h.	6	7	+	+	+			+		+
			8	8	+		+			+		+
6a	3954/37	Bc, cheek. Implantation: 8 n., 4 h.	7	4	+	+	+			+	+	+
6b	3954/37	Basi-squamous carcinoma in front of ear. Implantation: 6 n., 3 h. 40 min.	6	11	+	+	+		+	+	+	+
7	5618/37	Bc, cheek. Implantation: 6 n., 3½ h.	7	3	+	+	+			+	+	+
8	8314/39	Bc, cheek. Implantation: 10 n., 3¾ h.	1	7		+		+	+	+		
			5	2		+		+		+	+	+
9	5443/37	Bc, temple. Implantation: 11 n., 3 h.	7	5	+			+		+	+	+
10	7759/36	Bc, cheek. Implantation: 9 n., 3½ h.	8	10	+			+		+		+
			9	3		+		+		+	+	+
11	5818/38	Bc, cheek. Implantation: 13 n., 3¾ h.	8	2	+			+		+	+	+
12	10806/42	Bc, lid. Implantation: 5 n., 4 h.	4	1	+	+		+	+	+	+	+
13	1486/22	Recurrence of an operated cancer in front of left ear. Radium mould: skin dose about 20,000 r.	3	9	+	+	+			+		
		24 years later teleradium, 3,600 r against 2 fields, because of suspicions of recurrence with metastasis in lymph node.	24	1	+	+		+		+	+	+
14	5132/38	Basi-squamous carcinoma, forehead. Implantation: 5 n., 3¾ h.	8	4	+			+		+	+	+
15	13192/42	Basi-squamous carcinoma, nose. Implantation: 7 n., 3 h. 50 min.	4	1		+	+			+	+	+
16	11311/41	Bc, nose. Implantation: 8 n., 3 h. 40 min. After 5 years and 8 months: contact therapy, 8,000 r, against a nodule in the periphery of the scar.	5	8		+	+			+		+
17	7481/35	Bc, forehead. Implantation: 19 n., 4 h.	2	1	+	+		+	+	+		
			3	7	+	+	+			+		+
18	6066/36	Bc, behind ear. Implantation: 4 n., 4 h.	4	1	+		+			+		+
19	6331/35	Bc, submandibular region. Implantation: 19 n., 4 h.	3	11	+	+						
			5	1	+			+		+	+	+

Case No.	Record No.	Primary Tumour and Irradiation Treatment In all cases, except case 13 and case 23, radium needles were used, containing 10 mg Ra element and with a filter equivalent of 0.9 mm lead; active length 8 mm, diameter 2.3 mm. The distance between the needle axis was usually 4—5 mm.	Time elapsed after first irradiation		Clinical findings		Biopsy	Excision	Microscop. findings			
			Years	Months	Ulcer	Nodules			Recurrence	Degen connective tissue	Necrosis	Tubercle-like changes
20	13097/42	Squamous cell carcinoma, lower lip. Implantation: 8 n., 3 h. 50 min.	4	11	+			+		+		+
21	10185/42	Bc, cheek. Implantation: 8 n., 3¼ h. After 2½ years: contact therapy, 7,000 r, against a nodule in the periphery of the radium scar; no biopsy.	3	6	+	+		+		+	+	+
22	8148/37	Epitheliomatous naevus, capillitium. Implantation: 4 n., 3½ h.	9	10		+		+		+	+	+
23	5894/33	Fibrosarcoma, chest. Electro-excision + implantation: 8 6.4-mg and 1 3.2-mg needles, 15 h.	4	3	+			+		+		+
24	595/39	Bc, cheek. Implantation: 6 n., 3¾ h.	8	8	+		+			+	+	+
25	4726/27	Bc, lid. Implantation: 4 n., 4½ h.	19	10		+	+			+		+

In the area surrounding a carcinoma undergoing regressive changes, especially after irradiation treatment, tubercle-like structures sometimes appear (EWING, ENGLMANN, MCGREGOR). In our cases the structures have occurred several years after the irradiation and the disappearance of the tumour.

Material

For this investigation 26 cases of this peculiar type, appearing during the last ten years at Radiumhemmet, were collected. The sections were stained with hematoxylin-eosin, van Gieson, Weigert's elastic tissue stain and Ziehl-Neelsen's tubercle bacilli stain.

The primary tumours which had been irradiated were in most cases basal-cell carcinomas but other tumours were also represented. 25 cases had been treated by implantation of radium needles and 1 case by a radium mould. The dose in all cases had been what we may call a »skin carcinoma dose» or more. In several cases (nos. 2, 11, 13, 17 and 19) the doses had been remarkably large but in other cases they had been moderate. The clinical histories, treatments and microscopical findings are summarized in table 1. Concerning the dosage distribution and the technique of interstitial radium application at Radiumhemmet, the reader is referred to papers by SIEVERT, BENNER, MAGNUSSON and EBENIUS.

Fig. 1. Fig. 2. Fig. 3.

Fig. 1—3. Case nos. 15, 8 and 10. Nodules in the periphery of old radium scars clinically regarded as recurrences of basal-cell carcinomas. Microscopical examinations in all cases: irradiation changes with tubercle-like structures but no cancer.

The time interval between the first irradiation treatment and the initial examination of the specimens showing tubercular structures has varied from 3 to 24 years. In all cases but two, however, the changes appeared within 10 years after the treatment.

Microscopical Findings

In all cases, advanced irradiation changes of the usual type were found throughout the skin; namely, hyaline or fibrinoid degeneration and often necroses in the connective tissue, and also alterations of the blood vessels and epidermis.

The tubercle-like changes were mainly confined to the connective tissue of the corium and the subcutis. The changes were often found immediately beneath a non-ulcerated epithelium (fig. 4) but the deeper layers were also involved. In several cases tubercle-like structures were found in the fat tissue (fig. 8) and the striated muscles (fig. 10). In case 10 and case 13 rather large areas containing tubercular structures and necroses were found in the subcutaneous fat (fig. 6); none of these specimens showed lymph node structures. Often these changes were seen in the periphery of necrotic areas (fig. 5) but they were also found elsewhere (fig. 9). Tubercle-like foci were present in each case and in some cases there was also a rather diffuse infiltration by epithelioid cells. The tubercle-like foci were often surrounded by rings of lymphocytes (figs. 6, 8 & 10) or by fibrous capsules (fig. 9).

Fig. 4. Case 5. Tubercle-like nodule immediately beneath the atrophic epithelium. × 135.

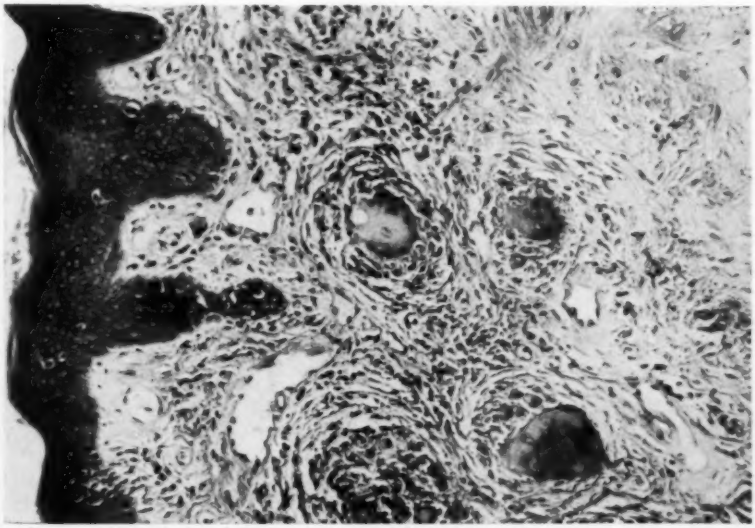

Fig. 5. Case 1. Tubercle-like granulation tissue with large giant cells in the periphery of a necrotic area. × 120.

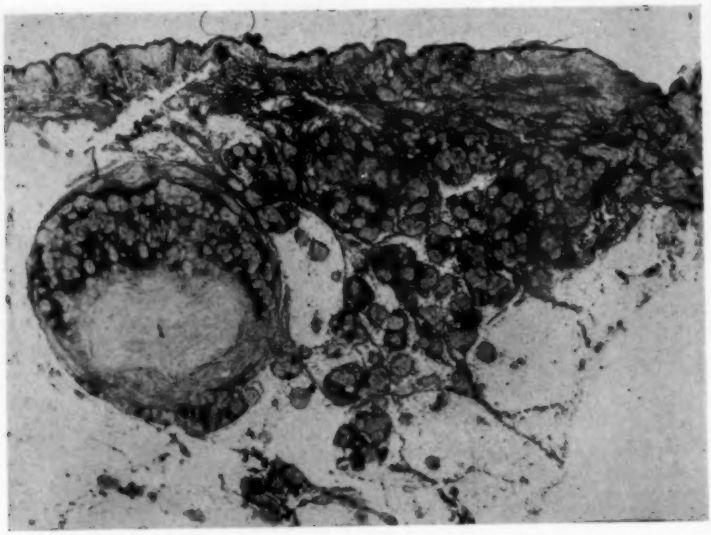

Fig. 6. Case 10. Tubercle-like changes throughout the skin. Large areas with tubercle-like changes and necrosis in the subcutaneous fat tissue. × 7.

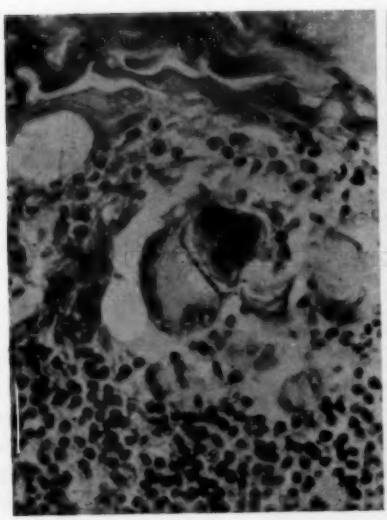

Fig. 7. Case 10. Giant cell with calcified inclusion. × 325.

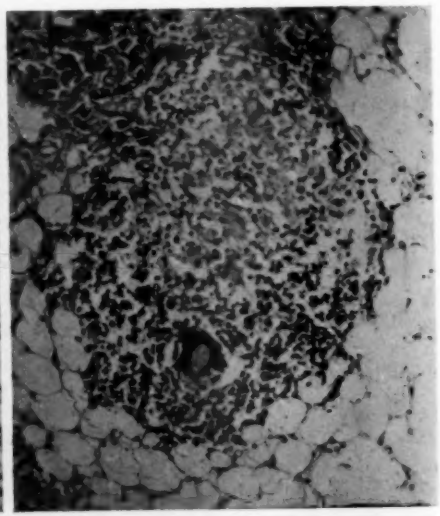

Fig. 8. Case 4. Tubercle-like structure in the subcutaneous fat tissue. Epithelioid cells, ring of lymphocytes and a giant cell of Langhans' type. × 120.

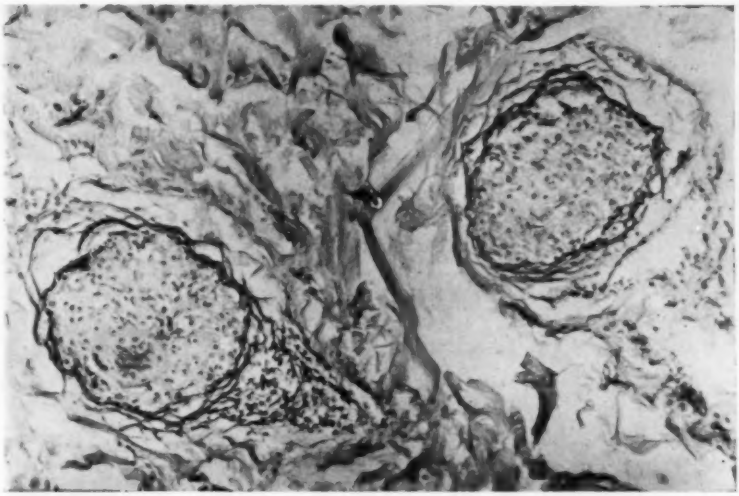

Fig. 9. Case 20. Two »tubercles» with epithelioid cells, giant cells and fibrous capsules. No lymphocytic rings. × 120.

The epithelioid cells closely resembled those found in tuberculosis. They were rather large acidophilic cells with an abundant cytoplasm which often had processes passing from one cell to another forming a sort of reticulum. Sometimes, however, the cells lay more compactly together. Giant cells both of Langhans' type and foreign body type were abundant. They were found especially in the centres of the tubercle-like foci, but also alone or in collections beside necrotic areas, or in connective tissue showing advanced degenerative changes. The giant cells of foreign body type often contained inclusions. These were most often rod-like, rather strongly refractive particles, unstained by van Gieson method. In one case round calcified particles (fig. 7) and strongly refractive, brown bodies were also found. The nature of these inclusions is obscure. In skin tuberculosis similar inclusions are often seen in the giant cells and are here derived from disintegrating and necrotic tissue, such as fragments of elastic and collagenous fibres and disintegrating blood cells. The inclusions in our cases probably have the same origin, but the possibility of foreign bodies brought into the tissue by the implantation must also be considered. In no case could tubercle bacilli be demonstrated in Ziehl-Neelsen stained sections.

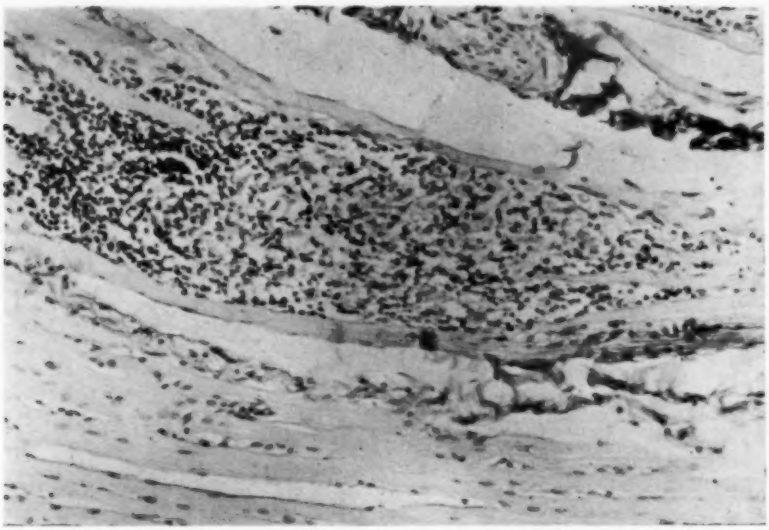

Fig. 10. Case 20. Tubercle-like structure in the striated musculature. × 160.

Discussion of Etiology

Epithelioid tubercles are by no means specific for tuberculosis. Similar structures also appear in syphilis, blastomycosis and several skin diseases of unknown etiology. They may also be found surrounding foreign body material and around necrotic tissue such as a carcinoma with regressive changes. Of interest is the experimental production of tubercular structures by injection of lipids from tubercle bacilli; certain long-chain organic acids are here believed to be the active agent (SABIN, ANDERSON a. o.).

The fact that tubercle bacilli were not found in the sections does not exclude a tuberculous etiology. It is often difficult to find the bacilli even in sections from proven tuberculous tissues and it is seldom possible in some of the tuberculids and in Morbus Schaumann (Boeck's sarcoid). Unfortunately, inoculation of fresh tissue material was not made in our cases. Clinical signs of a specific skin disease were, however, lacking in all cases. All the biopsy specimens from the primary tumours were examined; in many cases there were non-specific, inflammatory changes but in none were tubercular structures found.

Foreign body material may be brought into the tissue by the implantation of radium needles; for example, talcum powder from the gloves

may provoke foreign body granulomas. The needles are, of course, thoroughly cleaned and no fatty material is used for their preservation. No foreign bodies resembling talcum particles were found in the sections. The possibility of a foreign body reaction, however, can not be excluded but it is improbable that the often very extensive changes in our cases have this etiology.

During the progressive degeneration of connective tissue, foci of disintegrating tissue may act as »foreign bodies» or substances may be formed which are able to induce the formation of tubercle-like structures. The tubercle-like changes in our cases have an intimate connection with connective tissue undergoing advanced regressive changes or even necrosis. Substances able to induce tubercle-like structures may perhaps be absorbed by lymph vessels which would explain the deeper lying changes in some of the cases. Besides, it is probable that necroses, as in tuberculosis, secondarily appear in the tubercle-like foci. In almost all cases the changes appeared after implantation of radium needles. With roentgen treatment (or surface application of radium) the dose is greatest at the surface and then gradually diminishes. Thus the changes in the connective tissue are most pronounced in the superficial layers and when these changes are advanced enough we get an ulceration with detachment of necrotic material. With interstitial radium application, the heaviest dose is situated deeper in the dermis and foci with regressive changes appear in the deeper layers. Such foci may exist a long time without ulceration and may induce the formation of tubercle-like structures.

In this connection some experiments made by PULLINGER and PIRIE are interesting. They injected collagen extracted from ox cornea subcutaneously in rabbits and got microscopical changes rather like epithelioid tubercles. They believed that the changes were due to the relative insolubility of the injected collagen and they also believed that many of the chronic inflammations without infectious etiology »are due to alterations in the chemical state or physical relations of the host's own less soluble structures». Such alterations probably occur in the irradiated connective tissue.

Clinical Signification

In many of the cases nodules existed, which were clinically regarded as recurrences of the primary tumours. Fig. 1, 2 and 3 show such cases. In the first case the clinician had given a quite »classical» description of a basal-cell carcinoma. Fig. 4 shows a round tubercle-like focus lying immediately beneath the atrophic epidermis; the biopsy was taken from a small yellowish red nodule which clinically was regarded as a recurrence of a basal-cell carcinoma.

In the whole material, the specimens containing tubercle-like structures are derived from 29 biopsies or excisions, if we include only one excision from those cases where a biopsy and an excision had been made within a short interval. In the specimens from 2 of these excisions, recurrences or remnants of cancer existed as well as the irradiation changes. If we analyze the clinical examinations corresponding to the remaining 27 biopsies or excisions, we get the following result. Ulcerations existed in 20 examinations and in 10 of these the affection clinically looked like a necrotic ulcer; in the remaining 10 examinations nodules surrounding the ulcerations or hard elevated edges were found evoking suspicion of recurrence. In 7 examinations no ulcerations were found but there were small nodules clinically regarded as recurrences.

Sometimes irradiation treatment is given to a recurrence in the periphery of an old radium scar. Inasmuch as the changes described above often closely resemble recurrences of basal-cell carcinomas, a biopsy always ought to be taken before the irradiation.

The treatment of this special type of irradiation injury does not differ from the treatment of the necrotic ulcers which often coexist. In several cases the nodules disappeared spontaneously and the ulcers were often healed by conservative treatment. Sometimes, however, it was convenient to excise the whole involved area.

SUMMARY

Pronounced tubercle-like changes in late irradiation injuries of the skin are described in 26 cases. With one exception, they followed radium implantation. These changes are regarded as a peculiar type of tissue reaction due to advanced regressive changes in the connective tissue. Microscopically the changes closely resemble the granulation tissue in tuberculosis and clinically there are often small nodules which may be mistaken for recurrences of carcinomas.

ZUSAMMENFASSUNG

Ausgesprochene tuberkelähnliche Veränderungen sind in 26 Fällen bei Bestrahlungsspätschäden der Haut beschrieben. Mit einer Ausnahme folgten sie auf Radiumimplantation. Diese Veränderungen werden als ein durch vorgeschrittene Rückbildungsvorgänge des Bindegewebes bedingter, besonderer Typus von Gewebsreaktion angesehen. Mikroskopisch sind die Veränderungen dem tuberkulösen Granulationsgewebe sehr ähnlich, und klinisch kommen oft kleine Knötchen vor, die irrtümlich für Krebsrezidive gehalten werden können.

RÉSUMÉ

L'auteur décrit 26 cas où existaient, lors de lésions tardives de la peau causées par des irradiations, des modifications prononcées qui ressemblaient à la tuberculose. A une exception près elles étaient consécutives à l'implantation de radium. Ces altéra-

tions sont considérées comme un type particulier de réaction tissulaire dû à des modifications régressives au sein du tissu conjonctif: sous le microscope elles sont extrêmement semblables au tissu de granulation de la tuberculose, et cliniquement il y a souvent de petits nodules qu'on peut confondre avec des récidives de cancer.

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A METHOD OF BRONCHOGRAPHY[1]

by

Åke S. Gidlund

For some time past the Roentgen Department of St. Erik's Hospital in Stockholm has been using a bronchography instrument of new design. We ascribe the good examination results obtained partly to the fact that the new device makes possible successive anesthesia of the bronchi.

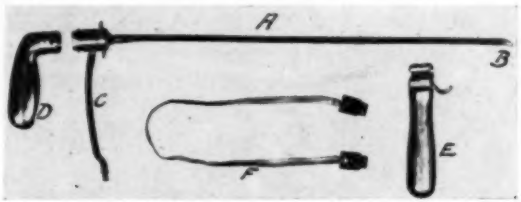

Fig. 1. The instrument for bronchography.

The instrument (Fig. 1) consists of the part which is introduced into the bronchi (A) — a tightly wound spiral of successively finer gauge stainless wire of a dimension which assures stability combined with sufficient flexibility in the outer part of the instrument. To avoid leakage of liquid etc. the spiral is covered with rubber. A bent mouthpiece (B), interchangeable, is threaded into the apex of the spiral in order to facilitate passage through the larynx and make possible introduction of the instrument into the bronchial branch concerned. There is an inlet (C) through which an anesthetic and contrast may be injected. The handle (D) has a bayonet mount which is released when the instrument is inserted. If desired, an auxiliary handle may be put on the spiral (E) to facilitate introduction of the instrument. The auxiliary handle is locked on when the catch in front is released, (F) is a band for fixation of the instrument.

[1] Submitted for publication, Nov. 27, 1948.

Fig. 2 a. The passage of the instrument through the larynx and injection of the anesthetic.

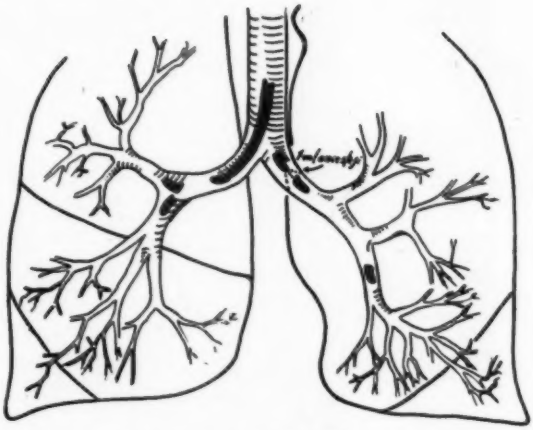

Fig. 2 b. The passage of the instrument through trachea and the bronchi and second injection of the anesthetic.

Since the contrast media for bronchography contain iodine, the patient must be tested for iodine sensitivity. (Potassium iodide is given per os for two days before the examination.) Should the patient prove hypersensitive the examination should under no circumstances be undertaken.

To prevent infectious complications in connection with the examination, the patient should be given penicillin before and additional afterwards. Three quarters of an hour before the examination 1 mg atropine is administered intramuscularly to reduce salivation and secretion in the bronchi, two factors which might have an adverse effect on the results. This quantity of atropine does not affect the patient's general condition.

Lest complications arise, oxygen, exadrine, and Narkotal for injection should be on hand throughout the examination.

Before examination the patient's blood pressure and pulse are checked. A bent spray is used to anesthetize the pharynx with 5 % cocain. A few minutes' pause follows to permit the anesthetic to take effect. Then the patient is placed behind the fluorescent screen with his right or left side facing it and during fluoroscopy the instrument is passed through

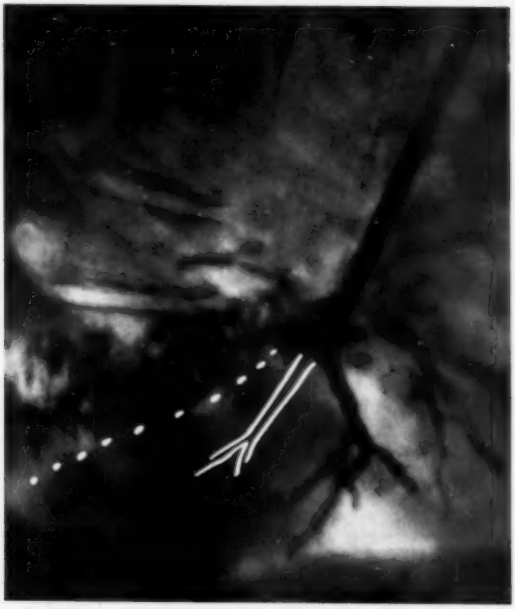

Fig. 3. Occlusion of the third ventral hyparterial bronchus (right lung).

the larynx as shown in fig. 2 a. When the mouthpiece has passed the larynx 2 ml of anesthetic are injected. (Xylocain Special, 2 %.)

Subsequently the patient is placed with his chest facing the fluorescent screen and the instrument is passed through the trachea. At the bifurcation the instrument is turned 90° to the right or left and comes down into the desired bronchus. Immediately below the bifurcation 1 ml of the anesthetic given above is injected into the bronchus to be examined. (Fig. 2 b.) (The total quantity of anesthetic in the bronchus should not exceed 4 ml.)

Following injection of the anesthetic in the trachea and the bronchus in question there must be a pause of 2—3 minutes to allow the anesthetic to take effect. Should the instrument be pushed down further too quickly, the patient might begin to cough and the anesthesia would then fail to produce the desired effect to some extent.

Thereafter the instrument is pushed on into the area to be examined. If the patient begins to cough, another 1 ml of anesthetic may be injected. When the lower lobes are examined the patient is placed with the diseased side facing the screen — this makes it easier to determine the

Fig. 4. Occlusion of the same bronchus by another patient with dislocation upwards of a small bronchus (white arrow) caused by a tumour.

Fig. 5. Saccular bronchiectasis in the lower lobe of the left lung (lateral view).

position of the instrument. In bronchography of the upper lobe areas it is well to place the patient in a supine position; the contrast will then fill out the bronchi and remain there.

Injection of contrast should take place slowly and during fluoroscopy so that the doctor may decide how much is required. Ordinarily about 5 ml is sufficient except when relatively large sections of lung must be examined (as in bronchiectasis).

In our examinations we have gone over to a highly viscous, easily resorbable contrast medium in preference to iodized oil, the use of which involves risk of fibrous induration in the lung parenchyma and greater danger of infection, since it remains so long.

In bronchography it is necessary to eliminate entirely the cough reflexes which arise when the contrast enters the bronchi. One cough is frequently enough to render the whole examination useless — partly, the

contrast is forced into the alveoli, partly it is coughed up out of the bronchi.

If anesthesia is used in the manner described above, injected via the bronchial instrument, the danger of coughing is entirely eliminated and other means of avoiding coughing which might affect the patient's general condition need not be used.

Another advantage of this instrument is that the examination may be carried out nearer to the part of the lung affected, and only the actual bronchial area need be filled with contrast. Thus the amount of contrast required is not so great. (This is demonstrated by the fig. 3, 4 and 5.)

The nearer to the diseased area the contrast medium may be injected, the shorter its transport distance will be, this lessens the danger of its carrying infectious material to the lung parenchyma (cf. injection of contrast via the nose or into the larynx).

When relatively large parts of the lungs are filled with contrast medium the danger of infection is increased. In addition, the actual area may be hidden by the contrast lying around it and a rather large volume of lung parenchyma be put out of respiratory action, at any rate for the time, being a condition which may be a contributing factor in dyspnea.

If the contrast is injected close to the area affected, conditions are more favourable for good filling, since the contrast pressure becomes greater (to some extent also because the mouthpiece of the instrument fills out the bronchial lumen).

SUMMARY

An instrument for bronchography which allows contrast filling of the bronchi close to the affection of the lung is described. The advantage of successive anesthesia of the bronchi is emphasized.

ZUSAMMENFASSUNG

Es wird ein Bronchographie-Instrument bechrieben, das die Kontrastfüllung der der Lungenaffektion benachbarten Bronchen ermöglicht. Der Vorzug einer nach und nach vorgenommenen Anästhesierung der Bronchen wird betont.

RÉSUMÉ

Description d'un instrument pour la bronchographie qui permet de remplir de substance opaque les bronches tout près de la lésion du poumon. L'auteur souligne les avantages d'une anesthésie successive des bronches.

FROM THE ROENTGENDIAGNOSTIC DEPARTMENT (HEAD: PROF. HANS HELLMER) AND THE LABORATORY FOR CLINICAL CHEMISTRY (HEAD: C. G. HOLMBERG, M. D.) OF THE UNIVERSITY CLINICS, LUND, SWEDEN.

ORAL HEPATOGRAPHY[1]

Preliminary Report of an Experimental Study

by

Olle Olsson and *Birger Ekman*

The provision of a method for the roentgen examination of the liver with contrast substance, hepatography, is a great desideratum.

In 1927 EINHORN and STEWART reported an increased density of liver and kidneys after intravenous injection of cholecystographic media.

Hepatography was performed with the use of Thorotrast (RADT 1929), with emulsified iodized fat (OSELLADORE and LENARDUZZI in animal experiments 1937) and with a sol of triiodostearate (DEGKWITZ, BECKERMANN a. POPKEN, 1938). Those substances, injected intravenously, were taken up by the reticulo-endothelial system, which is well represented in the liver. The liver was thus charged with contrast substance permitting hepatography.

DE NUNNO (1940) reports an accumulation of antimony in the liver and spleen after administration intravenously or per os of heavy doses of antimony tartrate to patients with malaria causing an increase in radiographic density of those organs lasting for months.

Thorotrast and triiodostearate have been in relatively extensive clinical use. The employment of Thorotrast had however to be abandoned owing to its deleterious effect on the cells. Neither was the triiodostearate suitable for routine hepatography (OLLE OLSSON, 1941). This contrast substance is no longer marketed.

In an endeavour to provide a method of hepatography one of us, OLLE OLSSON, began to study the radiopaque effect of various halogenated fat-emulsions on the liver, trying *a new and completely physiologic principle* for the charging of the liver with the contrast substance.

A brief report will be given of the preliminary results of experiments based on this principle.

[1] Submitted for publication, Oct. 28, 1948.

a b c

Fig. 1 a. Plain radiogram of a white rat.
Fig. 1 b. 33 hours after peroral administration of contrast medium: Liver markedly charged with contrast substance.
Fig. 1 c. About 36 hours later: The contrast medium has left the liver. Now a marked density is observable in the fatty layers of the shoulder muscles and in the fatty capsules of the kidneys.

Principle:

Fat entering the intestine is absorbed in the form of fatty acids. These fatty acids are then resynthesized, partly already in the intestinal wall, and partly in the liver. A great part of the fat fraction absorbed passes through the liver for subsequent combustion or storage in fat depôts. It is conceivable that if halogen be added to unsatiated fatty acids, a radiographic reproduction of the liver would be possible, provided these halogenated substances be absorbed in sufficient quantity, in an unchanged condition and be retained in the liver for a reasonable length of time.

Experiments with various halogenated oils seem to indicate that bromine is the halogen of choice, because it has the least effect on factors of importance for the absorption.

a b c

Fig. 2 a. Plain radiogram of a white rat.
Fig. 2 b. 33 hours after peroral administration of the contrast medium: Liver markedly charged with contrast substance.
Fig. 2 c. 24 hours later: Pronounced rarefaction of the contrast medium in the liver. Contrast medium now observable in the fatty layers of the pelvic musculature.

Method:

Quantities of 1—4 ml. brominated, emulsified oleum sesami (Research Lab., A. B. Leo, Hälsingborg) were administered orally by means of a tube to white rats. Roentgen-examinations were performed the following days.

Result:

After about 24 hours a rich accumulation of the contrast substance was observable in the liver. This accumulation lasted 2—12 hours after which it more or less quickly rarefied.

Simultaneously with the accumulation of the contrast substance in the liver and in association with the rarefaction of same a marked density

of the fatty capsule of the kidneys, the rest of the retroperitoneal fat, and of the fat depôts of the shoulder and pelvic regions could be noted.

A slight collection of contrast medium was also seen in the spleen owing to contrast-fat passing into the blood stream via the ductus thoracicus.

The experiments may be exemplified by the roentgenograms of two cases (see Figs. 1 & 2).

Preliminarily it has been proved that this physiologic principle permits experimental hepatography, that contrast radiography of the fat depôts is possible, and that stages of fat metabolism may be studied roentgenologically. Further the digestion of fat in the digestive tract can be studied with the contrast agents under discussion.

SUMMARY

A preliminary report of an experimental study of hepatography according to a new, completely physiologic principle, in which orally administered halogenated fatty acids pass through and fill the liver, which is thereby rendered radiopaque. The method also permits the radiographic reproduction of fat depôts and the roentgenological study of stages of fat digestion and metabolism.

ZUSAMMENFASSUNG

Vorläufiger Bericht über eine experimentelle Studie über Hepatographie nach einem neuen, durchaus physiologischen Prinzip, bei dem oral verabreichte Halogensalze von Fettsäuren durch die Leber gehen und diese füllen, wodurch sie röntgenundurchlässig wird. Die Methode erlaubt auch röntgenographische Wiedergabe von Fettdepots und röntgenologisches Studium der Stadien der Fettverdauung und des Fettstoffwechsels.

RÉSUMÉ

Rapport préliminaire sur une étude expérimentale de l'hépatographie exécutée selon un nouveau principe, complètement physiologique: des acides gras halogénés, administrés par voie buccale, passent par le foie et le remplissent, de sorte qu'il devient opaque aux Rayons X. La méthode permet aussi la reproduction radiographique de dépôts graisseux, et l'étude radiologique des stades de la digestion des graisses et de leur métabolisme.

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ON DOUBLE RENAL PELVIS AND URETERAL CALCULUS[1]

by

Selmer Rennæs

The radiographic picture during an acute attack of renal or ureteral calculus is now well recognized. From the Scandinavian countries the publications by HELLMER, WULFF, and ARNESEN have contributed greatly in this field. The Lund method, as advanced by HELLMER and WULFF, has proved very reliable and is now generally adopted.

In the case of single renal pelvis and acute ureteral calculus there is probably nothing to be added. However, duplication of the renal pelvis involves certain deviations from the usual picture and some observations made concerning double renal pelvis and ureteral calculus are considered as meriting some attention.

The radiographic examination in the case of double renal pelvis during an acute attack of ureteral calculus primarily reveals the anatomical conditions, but valuable information as concerns the excretion may be obtained as well.

From Drammen Hospital, NATVIG (1939) has published a case of calculus in one of the double ureters as observed during an acute attack. The radiographic examination revealed normal excretion into one renal pelvis but no excretion into the other homolateral pelvis where the stone occluded the ureter. NATVIG mentions nothing about accumulation of contrast medium in the corresponding part of the excreting renal parenchyma.

HELLMER, in a publication on nephrography (1943), has presented roentgenograms from a similar case. The excretion of contrast medium into the affected part of the urinary tract was markedly delayed, and after 70 minutes there was a distinct accumulation of contrast medium in the corresponding upper renal pole. At this juncture the contrast medium excreted into the homolateral lower renal pelvis had emptied

[1] Submitted for publication Nov. 18, 1948.

through the free ureter. HELLMER draws attention to the resemblance to the nephrogram which may be encountered in the case of renal tumor.

At the Roentgen Department of Oslo Municipal Hospital the material from the period 1945—1947 has been surveyed. During this three-year period 3,279 urographies were performed, and 49 cases, *i. e.*, 1.5 per cent, of double pelvis were detected. In 10 cases ureteral calculus was found on the same side as the double renal pelvis. Of these 10 cases 2 had previously had ureteral calculus on the opposite side where no duplication was present. In two other cases without calculus on the same side as the double renal pelvis, stone had been present on the opposite side and on this side only. There were 28 females and 21 males with duplication of the renal pelvis, whereas 2 females and 8 males had stone on the same side as the double renal pelvis. Thus it seems, that if there is a predisposition to calculus this probably shows only slight predilection to the same side as the double pelvis. The usual male preponderance of ureteral calculus is also seen in this material of double renal pelvis. This agrees with the conclusion reads by JOHANNIG from a study of the literature, namely that the double kidney shows only a slightly increased morbidity.

The 10 patients were all examined during an acute attack, and the excretory conditions can thus be studied from the urograms.

The Radiographic Picture

In order to be able to interpret the urograms, some knowledge regarding the anatomical variations is necessary. The primary feature is the duplication of the renal pelvis the two parts of which must always be *completely separated*. The kidney and the ureter may be more or less separated. An anatomical division of the kidney into two separate portions is a rare occurrence, whereas a complete duplication of the ureter (ureter duplex) is more frequently encountered. The question whether there is only a bifid pelvis or whether there is also a partial duplication of the ureter (ureter fissus) may, under certain circumstances, be a matter of opinion. However, the anatomical condition is usually distinctly revealed on the roentgen film, in some instances even better than on the patho-anatomical specimen. Otherwise the radiographic picture depends on the location of the stone.

I. If, in the case of ureter fissus (4 cases), the stone is situated in the common ureter the radiographic examination shows a delayed excretion in both renal pelves, contingently with accumulation of contrast medium in the entire kidney. The delayed secretion is the same in *both* homolateral renal pelves and the accumulation is confined to the *entire* kidney. A large kidney (14 by 7 cm, 15 by 7.5 cm) should arouse suspicion of a

Fig. 1 a. Case 1. Nephrogram showing a small left kidney. Retrospectively an upper rounded and a lower square shadow were distinguished.

double renal pelvis, particularly if this is found on the opposite side (2 cases). Except for the anatomical anomaly the urogram does not deviate from that obtained in the case of single renal pelvis with ureteral calculus.

One of the cases merits special mention as both excreting portions of the kidney are revealed in the nephrogram.

Case 1. E. B., female, aged 25.

During the past ten years prior to the admission the patient had suffered repeated attacks of abdominal pain. The duration of these attacks varied from some minutes to twenty-four hours. The attacks sometimes came on during the night. At the age of 22 she developed a pyelitis, which was treated by administration of the usual chemotherapeutic drugs. At the age of 24 she had a repeated attack with colicky pain in the left hypochondrium. The following days she was running a fever which varied from 37.7 to 39° C. Radiographic examination showed a stone in the lower part of the left ureter and no excretion on this side. An ureterolithotomy was performed. After the operation she was healthy for a year. Three weeks prior to the last admission she had repeated attacks like those she had suffered previously.

Fig. 1 b. Case 1. The kidney cut open. Ureter fissus.

Fig. 2. Case 2. Normal excretion into the upper renal pelvis. Delayed excretion into the lower renal pelvis. Concrement in the lower ureter (5 minutes).

The radiographic examination showed that the excretion was normal on the right side. On the left side, however, no contrast medium had been excreted after 5 minutes, but after 15 minutes there was accumulation of contrast medium showing a hypoplastic kidney (Fig. 1 a). A retrograde pyelogram the next day revealed a partial duplication of the ureter. No concrement could be seen on the roentgen films. However, the urine was not systematically examined for stones or stone fragments. However, the history and the urogram indicated ureteral obstruction probably caused by a calculus, and the case has been registered according to this. A nephrectomy was performed four days later. The kidney was small and measured 6 by 2.7 by 2 cm. The renal pelvis was duplicated and so was the ureter in a lenght of 3 cm. The specimen is shown in Fig. 1 b.

After the operation a closer study of the nephrogram revealed a bisection of the renal shadow as indicated by the arrows in Fig. 1 a. A rounded upper portion and a square lower portion are seen. By comparing the nephrogram and the photograph taken of the specimen it will be seen that the two shadows correspond to the tissue surrounding each of the homolateral renal pelves. A plain film showed no definite renal shadow, and in the specimen the thickness of the kidney is the same in the upper and lower poles. The shadow seen in the urogram is due to accumulation of contrast medium, and the borderline marks the two separate excreting portions. Despite the fact that there was no macroscopical bisection of the kidney, two separate excreting portions can be distinguished on the nephrogram. The cut surface only vaguely incidates a borderline.

II. When the stone is situated in one of the branches of a ureter fissus (4 cases) or ureter duplex (2 cases) the delayed excretion or contingent accumulation of contrast medium is always localized to the corresponding portion of the kidney as shown in the two cases presented below.

Case 2. G. N., female, aged 50.

Two days prior to the admission the patient suddenly experienced colicky pain in the left lumbar region. The attack lasted for three hours and then gradually ceased. Two days later she suffered a repeated attack, and was admitted to the hospital. The roentgen examination (Fig. 2) revealed a large left kidney (15 by 7.5 cm). The excretion into the upper renal pelvis was normal and there was free passage to the bladder. In the lower renal pelvis the excretion was delayed, but no definite accumulation of contrast medium could be seen. On the roentgenogram a concrement could be seen at the lower

Fig. 3 a. Case 3. Left kidney. Normal excretion into the upper renal pelvis and through a narrow ureter. Concrement in the minor pelvis near but outside the upper ureter.

Fig. 3 b. Case 3. Local accumulation of contrast medium in the lower pole of the kidney (15 minutes).

end of the ureter just below the transverse processus of L III. A roentgenogram taken after two and a half hours showed retention of contrast medium in the lower renal pelvis whereas the upper pelvis was empty.

Case 3. L. K., male, aged 49.

At the age of 46 the patient suddenly experienced intense pain in the right part of the abdomen. The pain radiated from the back and downwards into the right iliac fossa. The radiographic examination showed that there was no excretion on the right side and duplication of the left ureter but free passage on this side. Three years later he suffered a repeated attack, but this time the pain occurred on the left side. The radiographic examination (Fig. 3 a) showed normal excretion into the upper renal pelvis and free passage to the bladder through a thin ureter. In the minor pelvis just beside the upper ureter a small density indicating a calculus was seen. However, a gradual accumulation of contrast medium occurred in the lower pole of the kidney (15 minutes), the corresponding renal parenchyma taking the appearance of a circular well defined shadow (Fig. 3 b).

In both these patients the excretion was compromized corresponding to the occluded ureter but not in free portion of the kidney. This finding was the same in all the six cases. WULFF has previously carried out a

thorough study of reflex calculous anuria which he defines as »a total anuria caused by blocking of only *one* ureter by a calculus, the stimuli from this ureter acting reflexly on the other entirely healthy kidney in such a manner that its secretion of urine is completely inhibited». Based on clinical and experimental data he concludes: »We believe that we are justified in maintaining that if reflex calculous anuria occurs at all — which is doubtful — it is extremely rare and is of no practical importance.»

It must be assumed that if a reflectory suppression occurs in the case of double renal pelvis, it would most likely be more marked on the homolateral than on the contralateral side. However, the normal excretion through the homolateral non-occluded ureter also seems to be contradict such a thing as a reflex anuria.

In these six cases marked accumulation occurred in one instance only. In this case the borderline stands out clearly on the roentgenogram, but it will scarcely always be sharply outlined. The two excreting portions may be separated by a slantly directed fibrous strand or one portion may cover the other like a cup. Under such circumstances the separate portions cannot be sharply distinguished on the roentgen film.

As regards the differential diagnosis case 3 merits attention. After 5 minutes no definite accumulation of contrast medium in the lower pole could be seen. On the contrary, the passage from the upper renal pelvis was free. There is thus the possibility of overlooking the accumulation if the urography is not performed lege artis according to the Lund method, *i. e.*, if not a contingent delayed accumulation is considered. In that case one may primarily be puzzled why there is no urinary retention. NATVIG, in his publication, has mentioned this possibility of overlooking the stenosis and the delayed excretion.

Conclusion

In these cases urography has proved to be a valuable method. The principal changes including delayed excretion and accumulation of contrast medium corresponding to the occluded ureter, are found to be the same as in the case of single renal pelvis and acute ureteral calculus. The urography revealed no facts whatever in support of the existence of a ureterorenal reflex acting on the portion of the kidney corresponding to the homolateral non-occluded ureter.

SUMMARY

Among 3,279 urographies double renal pelvis was encountered in 49 cases, *i. e.*, in 1.5 per cent. In 10 patients ureteral calculus occurred on the same side as the double pelvis. When the stone is situated in the common ureter the excretion of contrast medium

is compromized in the entire kidney. In a single instance the two excreting portions were revealed on the nephrogram. A stone in one of the branches of a double ureter will cause a delayed secretion, or an accumulation of contrast medium in the renal parenchyma corresponding to the occluded branch. No facts whatever have been revealed in support of the existence of a homolateral reflex calculus anuria to the non-affected portion of the kidney.

ZUSAMMENFASSUNG

Unter 3,279 urographierten Fällen kam 49-mal doppeltes Nierenbecken vor — 1.5 %. 10 Fälle zeigten homolateral Ureterstein. Bei 10 Patienten kam ein Ureterstein auf der Seite des doppelten Nierenbeckens vor. Wenn der Stein im gemeinsamen Ureter sass, war die Ausscheidung in der gesamten Niere herabgesetzt und verzögert. In einem einzelnen Falle wurden die beiden sezernierenden Teile auf dem Nephrogram beobachtet. Stein im einen Doppelureter gab herabgesetzte und verzögerte Ausscheidung oder Auffüllung mit Kontrastmittel nur im zugehörigen occludierten Teil. Keine Anhaltspunkte für homolaterale uretero-renale reflektorische Steinanurie des nicht-affizierten Teiles der Niere.

RÉSUMÉ

Sur 3,279 urographies on a rencontré 49 fois un bassinet double, c'est-à-dire dans 1.5 % des cas. Chez dix malades il y avait un calcul uretéral du même côté que le double bassinet. Quand le calcul est situé dans l'uretère commun, l'excrétion de la substance de contraste est compromise dans le rein tout entier. Dans un seul cas les deux parties sécrétantes du rein furent visibles sur le néphrogramme. Une pierre dans l'une des deux branches d'un uretère double entraînera un retard de la sécrétion, ou une accumulation de la substance opacifiante dans le parenchyme rénal correspondant à la branche occluse. Aucun fait quelconque n'a été observé qui vienne confirmer l'existence d'une anurie calculeuse par réflexe homolatéral dans la partie indemne du rein.

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CHOLECYSTOGRAPHY AND THE SURGICAL FINDINGS[1]

by

Olallo Morales and *Jörgen Swedberg*

In the statistical study of the cases of biliary calculi of the surgical department of the Norrköping Hospital it was found that the roentgen diagnosis did not always correspond to the surgical findings (1). In a cooperative study with the roentgen department the roentgen findings in 546 cases in which cholecystography and cholecystectomy were performed between the years 1934—1947 were compared with the final diagnosis after surgery. Only those cases in which the roentgen examination was performed no longer than a few weeks before operation were included in the study.

During these 14 years the technique of the roentgen examination has not varied significantly. Following emptying of the gall bladder after administration of a fatty meal the biliary contrast was given per os. The contrast material has varied. At the onset preparations of tetraiodophenolphthalein such as jodeikon, jodafen, cholotrast were used and in the last years biliselectan and Priodax. The examination was undertaken with a scout film of the gall bladder area in prone position. On this film the degree of concentration of the dye in the gall bladder was determined. Thereafter the examination was continued in upright position according to the well known method of Åkerlund with use of small fields in varying projections. On these films one observed the size and position of the calculi possibly present and the movements of the gall bladder during respiration and any other pathological process in the viscus or in the adjacent region. Following this procedure the patient was administered the fatty meal and again filmed in 2 hours. Here the contraction of the contrast filled gall bladder and the concentration of the dye was again studied.

[1] Submitted for publication, Nov. 17, 1948.

Those cases in which examination was considered unsatisfactory because of vomiting, diarrhea, gas and other bowl contents overlying the gall bladder region, were reexamined. If the study was again unsatisfactory the case was excluded from this review.

In survey of the literature in the years 1933—1947 one finds a rather marked variation in statistical studies comparing the roentgen and the operative findings.

Representative Statistical Comparative Studies

	Year	Number of cases	Agreement
Radojevic (13)	1934	416	90 %
Schrader (2)	1935	61	93 %
Johnson & Harrel (5)	1935	32	97 %
Collins & Root (6)	1935	149	93 %
Pendergrass & Hodes (14)	1935	70	97 %
Hodges & Lamp (3)	1937	186	94 %
Good & Kirklin (15)	1937	104	98 %
Colp (16)	1937	108	94 %
Friedman & Friedman (9)	1938	81	91 %
Olsson (17)	1939	292	97 %
Levyn & Meyers (9)	1940	54	40 %
Doran a. o. (19)	1941	147	c:a 90 %

As is evident the average carefully performed statistical studies show agreement in over 90 % of cases. Most authors indicate no difference between the oral and intravenous administration of the contrast (2, 3). The oral route is the method of preference inasmuch as untoward effects such as severe vomiting, fall of blood pressure and hypersensitivity reactions, frequently occur following intravenous injection of the contrast. Two cases in a series of 6,000 examinations with intravenous contrast were fatal (4, 5). Some authors perform intravenous cholecystography in those cases in which no filling or poor filling of the gall bladder is found after oral administration (6, 7, 8). The majority of the other investigators do not depend on this intravenous check examination but prefer a repeated cholecystography with either the same dose, a double, or a triple dose of the same contrast or with an other preparation. Thus Friedman & Friedman (9) have demonstrated that in 472 cases there was failure of filling the gall bladder in the initial examination with oral contrast in 112 of these. However, in the follow-up examination with the same dose of the same contrast material they obtained good filling in 99 cases of the same 112. Similar experiences have been observed by other investigators (3, 5, 9, 10, 11, 12). On the other hand cases have been reported in which no filling of the gall bladder was observed after intra-

venous injection of the dye, but at a later date good filling was observed after the oral administration of the contrast.

In this series the comparision of the roentgen to the operative findings was complicated in some cases inasmuch as a detailed operative report was lacking. Difficulty was encountered in invariably determining the diagnosis of chronic cholecystitis. Some cases were encountered in which the histological diagnosis was made but which at operation a grossly normal appearing organ was revealed, with only a few loose adhesions and in which no great disturbance of the function of the gall bladder was evident. By the term chronic cholecystitis used in our table we have included those cases in which (a) microscopic findings were present, (b) thickened wall and adhesions to the gall bladder or (c) a shrunken fibrotic gall bladder were found.

In the same table the concretions are classified as follows: »large stones» — greater than a pea, and »small stones» — less than pea size. The quantity of stones was not considered because it seemed to have little practical significance in this consideration.

Table I

Roentgen findings	Operative findings																		Totals
	Normal gall bladder				Acute cholecystitis				Chronic cholecystitis				Cholesterosis				Other findings		
	without stone	with small stones	with large and small stones	with large stones	without stone	with small stones	with large and small stones	with large stones	without stone	with small stones	with large and small stones	with large stones	without stone	with small stones	with large and small stones	with large stones			
Normal filling of the gall bladder																			
without stone	4	2			1				5	1			2						15
with small stones		12	3	3										4					22
with large and small stones			3	1			1				6	1		1					13
with large stones		1	2	14			2	2			2	2				2			27
Thin contrast filling																			
without stone	2	2	4	4	2	1	1	4	2	3	4	5	2			1	1		38
with small stones	7	3								6									16
with large and small stones			4			1				1	5								11
with large stones			2	11			1	2			9	10							35
No contrast filling																			
without stone	12	31	33	20	4	18	20	27	24	31	27	43	5	1	1	2	4		303
with small stones		3								6	1								10
with large and small stones			3	1			2				5								11
with large stones		1	3	7			1	6			6	19				1	1		45
Totals	25	55	57	61	7	20	28	41	31	48	65	80	9	6	1	6	6		540

In the series there were 77 cases in which roentgen examination demonstrated *normal contrast filling*, and concretions were evident on the films in 62 of these cases, all of which were verified at operation. In 15 of the same 77 cases demonstrating no pathological change in roentgen examination, at surgery concretions in form of gravel were found in 3 cases, cholecystitis without concretions in 6 cases and cholesterosis in 2 cases. The remaining 4 cases were operated in spite of normal roentgen findings because of other clinical indications (one was thought to be a chronic typhoid carrier). The gall bladder of these 4 cases showed no pathology in the operative specimen.

With contrast filling in the gall bladder it is possible that stones with the same density as the contrast may escape detection, and only make themselves evident under fortuitous circumstances. This has occurred in one case in the series. For this reason scout films of the gall bladder region may be indicated before the contrast is administered.

Thin density of the dye in the gall bladder was encountered in 100 cases. In 62 of these roentgen examination demonstrated concretions. Confirmation was found at surgery in 55 cases. The other 7 were normal. In 38 cases roentgen revealed no concretions, but in 29 of these, stones were demonstrated at operation. In the remaining 9 cases out of these 38 the operative findings, as the roentgen findings demonstrated no stones. Herein the gall bladder was normal in 2 cases, 2 cases showed acute cholecystitis, 2 demonstrated chronic cholecystitis and 2 cholesterosis. In one case the impaired gall bladder function could be attributed to a lymphadenitis at the cystic duct which was found present.

In the 369 cases in which the roentgen examination demonstrated *no contrast filling* the roentgen examination and the operative findings demonstrated stones in 65 of this group. In one case the diagnosis of concretions was made by roentgen but at surgery no stone was found in the biliary tract but a calcified lymphadenitis adjacent to the cystic duct. In the 303 cases in which there were no visible stone on the roentgen films concretions were found at surgery in 254 cases (*84* %) while 37 cases demonstrated other pathological conditions in or adjacent to the gall bladder. Twelve cases revealed an entire normal gall bladder.

In 22 cases cholesterosis was found in the operative specimen. As the etiology of this condition has not yet been fully clarified whether it is due to an inflammatory reaction following chronic cholecystitis or a physiologic variation of the cholesterin metabolism are two theories offered (20). We have chosen to count it as an inflammation in the conclusions that follows, but we have made a special classification in the table. Of these 22 cases at roentgen examination 9 showed normal contrast filling of the gall bladder, while 3 had a thin and 10 no contrast in the viscus.

Conclusions

A. *On the basis of the surgical findings.*

I. When concretions were found in an otherwise normal gall bladder (173 cases) roentgen revealed

normal contrast filling	in	41 cases	(*23½* %)
of which there were concretions	in	39 cases	(*95* %)
thin contrast filling	in	30 cases	(*17½* %)
of which there were concretions	in	20 cases	(*66½* %)
no contrast filling	in	102 cases	(*59½* %)
of which there were concretions	in	18 cases	(*17½* %)

II. When inflammatory changes in the gall bladder were found without concretions (47 cases) roentgen revealed

normal contrast filling without concretions	in	8 cases	(*17* %)
thin contrast filling without concretions	in	6 cases	(*13* %)
no contrast filling without concretions	in	33 cases	(*70* %)

III. When inflammatory changes in the gall bladder were found together with concretions (295 cases) roentgen revealed a pathological condition in the gall bladder in *99.7* % of which there was

normal contrast filling	in	24 cases	(*8* %)
thin contrast filling	in	54 cases	(*18½* %)
no contrast filling	in	217 cases	(*73½* %)

B. *On the basis of the roentgen findings.*

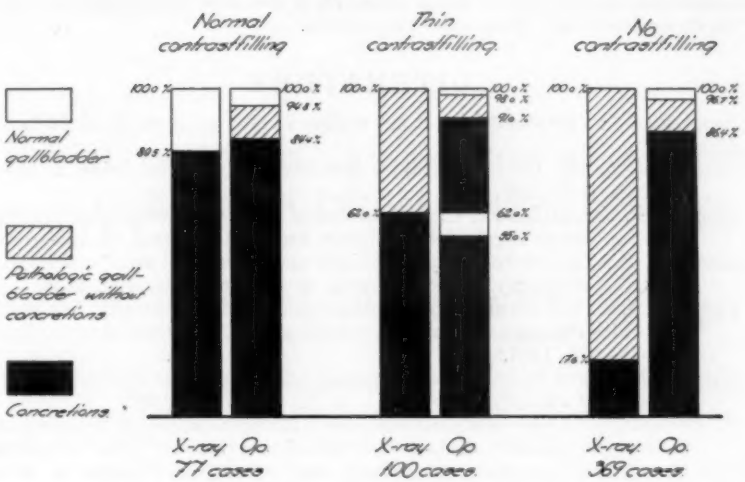
I. With the roentgen findings of »thin contrast filling» of the gall bladder without evidence of concretions (38 cases) the surgical findings were

concretions with or without inflammation	in	29 cases	(*76* %)
only inflammation	in	6 cases	(*16* %)
normal gall bladder	in	2 cases	(*5½* %)
other findings	in	1 case	(*2½* %)

II. With the roentgen findings of »no contrast filling» of the gall bladder without evidence of concretions (303 cases) the surgical findings were

concretions with or without inflammation	in	254 cases	(*84* %)
only inflammation	in	33 cases	(*11* %)
normal gall bladder	in	12 cases	(*4* %)
other findings	in	4 cases	(*1* %)

Table II



SUMMARY

The authors compared the cholecystographic diagnosis with the operative findings in 546 cases, in which the surgery was performed within a few weeks after the roentgen examination. The greatest deficiency between roentgen and operation findings was present in »thin» and »no» contrast filling of the gall bladder at roentgen examination. Therefore it is of utmost importance to obtain the best possible filling of the gall bladder by repeated administration of the dye or increased dose of the same or of another preparation.

ZUSAMMENFASSUNG

An 546 Fällen, bei denen innerhalb von wenigen Wochen nach der Röntgenuntersuchung ein chirurgischer Eingriff vorgenommen wurde, vergleicht Verf. die cholezystographische Diagnose mit dem Operationsbefunde. Die grösste Unstimmigkeit zwischen röntgenologischen und operativen Befunden sah man bei »dünner» oder »fehlender» Kontrastfüllung der Gallenblase bei der Röntgenuntersuchung. Es ist deshalb von ausserordentlicher Bedeutung, die bestmögliche Füllung der Gallenblase zu erzielen durch wiederholte Verabfolgung der gleichen oder einer grösseren Dosis von demselben Kontrastmittel oder einem anderen Präparat.

RÉSUMÉ

Les auteurs ont comparé le diagnostic cholécystographique avec les trouvailles opératoires dans 546 cas où l'acte chirurgical fut exécuté au plus tard quelques semaines après l'examen aux Rayons Roentgen. Les plus nombreuses erreurs radiologiques, révélées ensuite par les constatations opératoires, étaient commises lorsque le remplissage de la vésicule donnait une image »faible», ou pas d'image du tout. Aussi est-il

d'une extrême importance d'obtenir le meilleur remplissage possible de la vésicule par l'administration répétée de la même dose, ou d'une dose plus forte, soit du même produit de contraste, soit d'une autre préparation.

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FROM THE DANISH CANCER REGISTRY UNDER THE NATIONAL ANTI-CANCER LEAGUE, COPENHAGEN, DENMARK (DIRECTOR: JOHANNES CLEMMESEN, M. D.)

AGE DISTRIBUTION FIGURES FOR MALIGNANT DISEASES IN DENMARK 1942—1944[1]

by

Johannes Clemmesen, M. D., *Thøger Busk*, Lic. act., and *Arne Nielsen*, Lic. act.

Curves giving the age distribution of malignant diseases of various site were published in Acta Radiologica Vol. XXX pag. 9—16 1948 and total numbers for cancers of various site in Vol. XXIX pag. 321—330.

For practical clinical work it is more interesting to know the factual frequency with which malignant diseases are met in various age classes, and this will be given in the following together with the relative frequencies computed on the basis of the census figures for July 1st, 1943. A statement with regard to the incidence of cancer among children in Denmark has already been given by VIDEBÆK, on the base of these figures.

In using the figures it should be remembered that the age given refers to the time of the first admission in hospital, and, for patients known through death certificate only, the time of death. The consequences of this have been dealt with in the papers previously mentioned.

The earliest material of a cancer registry will always be less correct than materials collected at a later date, because cancer patients that are under treatment at the start of the registry in spite of all measures are only gradually notified to the registry, and thus to some extent indistinguishable from fresh cases, which alone will give a reliable expression of cancer incidence among the population in question.

However, for most practical purposes our figures will be sufficiently correct, as we have endeavoured to exclude all cases admitted in hospital earlier than Jan. 1942.

The following tables comprises those sites of cancer that are sufficiently frequent to yield a material of some size in the course of three years.

It is well worth mentioning that most statements from other countries at the present time will deal with mortality from cancer, so that direct

[1] Submitted for publication, Nov. 20, 1948.

comparisons will not be possible with the present figures. For such purposes, the figures published by the Danish Health Service will be useful.

Tumours stated as sarcomata, and cases of uncertain site or uncertain malignity have been grouped separately. The same applies to tumours known only by metastases. This does not exclude that cases of sarcoma, labelled as malignant disease, but without histological examination may figure as cancer.

Age Distribution of the Danish Population 1/7 1943

Age		Sarcomata (Tumours indicated as such).			Cas. malignitat. incert.			Cancer colli uteri		
		Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males										
0—4	176 800	16	—	0.30	2	2	0.08	—	—	—
5—9	154 500	4	—	0.09	3	1	0.09	—	—	—
10—14	150 700	11	1	0.27	2	—	0.04	—	—	—
15—19	160 800	17	1	0.37	6	—	0.12	—	—	—
20—24	167 300	16	2	0.36	3	1	0.08	—	—	—
25—29	156 600	16	—	0.34	7	1	0.17	—	—	—
30—34	162 400	22	2	0.49	9	—	0.18	—	—	—
35—39	148 100	21	—	0.47	8	3	0.25	—	—	—
40—44	133 700	26	1	0.67	13	1	0.35	—	—	—
45—49	120 200	30	4	0.94	26	4	0.83	—	—	—
50—54	102 800	40	6	1.49	27	11	1.23	—	—	—
55—59	92 100	24	6	1.09	30	18	1.74	—	—	—
60—64	77 500	30	7	1.59	42	22	2.75	—	—	—
65—69	63 100	37	7	2.32	34	28	3.28	—	—	—
70—74	43 000	18	8	2.02	44	26	5.43	—	—	—
75—79	26 400	15	3	2.27	30	44	9.34	—	—	—
80—84	13 100	5	4	2.29	12	28	10.18	—	—	—
85—	5 880	8	1	5.10	3	12	8.50	—	—	—
Females										
0—4	169 400	8	1	0.18	—	6	0.12	—	—	—
5—9	149 800	5	—	0.11	2	—	0.04	—	—	—
10—14	147 700	9	1	0.23	—	—	—	—	—	—
15—19	157 800	12	4	0.34	1	1	0.04	—	—	—
20—24	164 400	10	—	0.20	6	—	0.12	4	—	0.08
25—29	157 300	12	2	0.30	5	1	0.13	63	—	1.34
30—34	163 600	10	—	0.20	9	1	0.20	148	—	3.02
35—39	152 500	28	—	0.61	14	—	0.31	198	4	4.42
40—44	141 100	25	2	0.64	17	8	0.59	274	3	6.54
45—49	128 000	30	1	0.81	16	6	0.57	268	1	7.01
50—54	109 900	23	2	0.76	38	8	1.40	201	1	6.31
55—59	99 400	35	9	1.48	32	11	1.44	177	1	5.97
60—64	83 300	39	1	1.60	39	14	2.12	120	4	4.96
65—69	67 200	34	5	1.93	31	43	3.67	80	3	4.12
70—74	48 100	28	6	2.36	39	50	6.17	56	1	3.95
75—79	31 000	18	12	3.23	29	71	10.75	28	3	3.33
80—84	16 400	9	4	2.64	18	62	16.26	11	2	2.64
85—	7 650	4	1	2.18	3	32	15.25	5	—	2.18

Age	Cancer corporis uteri			Cancer uteri non-spec.			Cancer ovarii			Cancer alior. organ. gen. fem.			Cancer mammae		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
25—29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30—34	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
35—39	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
40—44	—	—	—	—	—	—	—	—	—	—	—	—	1	—	0.02
45—49	—	—	—	—	—	—	—	—	—	—	—	—	2	—	0.05
50—54	—	—	—	—	—	—	—	—	—	—	—	—	1	—	0.03
55—59	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
60—64	—	—	—	—	—	—	—	—	—	—	—	—	3	—	0.11
65—69	—	—	—	—	—	—	—	—	—	—	—	—	1	—	0.04
70—74	—	—	—	—	—	—	—	—	—	—	—	—	3	1	0.21
75—79	—	—	—	—	—	—	—	—	—	—	—	—	5	—	0.39
80—84	—	—	—	—	—	—	—	—	—	—	—	—	—	1	0.13
85—	—	—	—	—	—	—	—	—	—	—	—	—	2	—	0.51
Females													1	—	0.57
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	2	—	0.05	—	—	—	—	—	—
20—24	2	—	0.04	—	—	—	6	—	0.13	—	—	—	—	—	—
25—29	4	—	0.08	—	5	0.11	5	—	0.10	1	—	0.02	2	—	0.04
30—34	9	1	0.20	2	6	0.16	10	—	0.21	3	—	0.06	7	—	0.15
35—39	17	—	0.37	—	3	0.07	18	—	0.37	3	—	0.06	58	2	1.22
40—44	23	—	0.54	2	11	0.31	34	3	0.81	5	—	0.11	106	6	2.45
45—49	62	—	1.61	3	8	0.29	53	8	1.44	12	3	0.35	218	11	5.41
50—54	89	1	2.73	3	18	0.64	76	10	2.24	8	1	0.23	309	33	8.91
55—59	99	2	3.39	7	24	1.04	73	7	2.43	12	2	0.42	244	33	8.40
60—64	71	1	2.88	3	21	0.96	74	18	3.09	17	—	0.57	330	42	12.48
65—69	61	1	3.08	3	32	1.74	59	12	2.84	17	1	0.72	325	46	14.85
70—74	39	2	2.84	5	29	2.36	50	10	2.98	21	1	1.09	316	64	18.85
75—79	16	1	1.83	2	23	2.69	29	11	2.77	13	—	0.90	208	67	19.06
80—84	10	—	2.03	1	13	2.85	17	13	3.23	13	1	1.51	115	62	19.03
85—	2	—	0.87	—	11	4.79	2	4	1.22	10	4	2.85	57	43	20.33
							5	—	2.18	3	—	1.31	21	34	23.97

Age	Cancer ventriculi			Cancer oesophagi			Cancer coli			Cancer coli sigmoid.			Cancer intestini[1]		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	1	0.02
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	1	0.02	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	3	—	0.06	—	—	—	—	—	—
20—24	—	—	—	—	—	—	1	—	0.02	1	—	0.02	—	1	0.02
25—29	6	—	0.13	—	—	—	3	1	0.09	—	—	—	1	—	0.02
30—34	12	2	0.29	2	—	0.04	5	—	0.10	3	—	0.06	—	1	0.02
35—39	23	1	0.54	—	—	—	14	2	0.36	1	1	0.05	2	—	0.05
40—44	49	9	1.45	2	1	0.07	4	1	0.12	5	—	0.12	1	—	0.02
45—49	83	19	2.83	8	1	0.25	20	4	0.67	13	—	0.36	3	—	0.08
50—54	141	28	5.48	5	2	0.23	27	3	0.97	20	3	0.75	5	—	0.16
55—59	200	49	9.01	34	5	1.41	46	9	1.99	27	3	1.09	7	3	0.36
60—64	289	85	16.09	48	8	2.41	67	16	3.57	33	—	1.42	8	6	0.60
65—69	340	153	26.04	72	16	4.65	58	21	4.17	60	3	3.33	8	12	1.06
70—74	243	219	35.81	63	23	6.67	74	50	9.61	34	2	2.79	11	18	2.25
75—79	165	236	50.63	40	38	9.85	32	46	9.85	33	5	4.80	6	16	2.78
80—84	55	153	52.93	24	16	10.18	18	37	13.99	20	3	5.85	2	21	5.85
85—	12	62	41.95	5	18	13.04	7	16	13.04	2	1	1.70	—	7	3.97
Females															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	1	—	0.02	—	—	—	—	—	—
20—24	3	1	0.08	—	—	—	2	—	0.04	—	—	—	1	—	0.02
25—29	1	—	0.02	—	—	—	3	—	0.06	5	—	0.11	1	—	0.02
30—34	13	2	0.31	2	—	0.04	9	—	0.18	1	—	0.02	1	—	0.02
35—39	25	5	0.66	2	—	0.04	11	1	0.26	7	2	0.20	—	1	0.02
40—44	31	8	0.92	2	—	0.05	11	2	0.31	12	1	0.31	1	—	0.02
45—49	56	17	1.90	9	—	0.23	21	4	0.65	19	1	0.52	4	—	0.10
50—54	80	28	3.28	7	3	0.30	30	6	1.09	27	—	0.82	2	3	0.15
55—59	126	40	5.57	10	3	0.44	51	10	2.05	34	1	1.17	4	6	0.34
60—64	159	80	9.56	16	—	0.64	68	31	3.96	42	4	1.84	4	5	0.36
65—69	210	138	17.26	27	6	1.64	59	36	4.71	23	3	1.29	9	19	1.39
70—74	184	235	29.04	24	17	2.84	55	63	8.18	28	5	2.29	8	26	2.36
75—79	90	294	41.29	19	18	3.98	47	64	11.94	15	4	2.04	5	33	4.09
80—84	33	228	53.05	17	19	7.32	22	68	18.29	6	2	1.63	1	17	3.66
85—	21	106	55.34	1	13	6.10	6	33	16.99	2	—	0.87	1	9	4.36

[1] C. intest. ten., C. duodeni, C. intest. non-spec.

Age	Cancer recti			Cancer hepatis			Cancer pancreatis			Cancer abdominis			Cancer labii		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
25—29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30—34	1	—	0.02	—	—	—	—	—	—	—	—	—	—	—	—
35—39	1	—	0.02	—	—	—	—	—	—	—	—	—	—	—	—
40—44	2	—	0.04	—	—	—	—	—	—	—	—	—	—	—	—
45—49	3	—	0.08	—	—	—	—	—	—	—	—	—	—	—	—
50—54	4	1	0.16	—	—	—	—	—	—	—	—	—	—	—	—
55—59	6	1	0.30	—	—	—	—	—	—	—	—	—	—	—	—
60—64	6	2	0.36	—	—	—	—	—	—	—	—	—	—	—	—
65—69	8	4	0.60	—	—	—	—	—	—	—	—	—	—	—	—
70—74	5	4	0.61	—	—	—	—	—	—	—	—	—	—	—	—
75—79	3	4	0.79	—	—	—	—	—	—	—	—	—	—	—	—
80—84	1	2	0.49	—	—	—	—	—	—	—	—	—	—	—	—
85—	—	1	0.49	—	—	—	—	—	—	—	—	—	—	—	—
Females															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
25—29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30—34	1	—	0.02	—	—	—	—	—	—	—	—	—	—	—	—
35—39	1	—	0.02	—	—	—	—	—	—	—	—	—	—	—	—
40—44	2	—	0.04	—	—	—	—	—	—	—	—	—	—	—	—
45—49	3	—	0.08	—	—	—	—	—	—	—	—	—	—	—	—
50—54	4	1	0.15	—	—	—	—	—	—	—	—	—	—	—	—
55—59	6	1	0.30	—	—	—	—	—	—	—	—	—	—	—	—
60—64	6	2	0.36	—	—	—	—	—	—	—	—	—	—	—	—
65—69	8	4	0.60	—	—	—	—	—	—	—	—	—	—	—	—
70—74	5	4	0.61	—	—	—	—	—	—	—	—	—	—	—	—
75—79	3	4	0.79	—	—	—	—	—	—	—	—	—	—	—	—
80—84	1	2	0.49	—	—	—	—	—	—	—	—	—	—	—	—
85—	—	1	0.49	—	—	—	—	—	—	—	—	—	—	—	—

[1] C. intest. ten., C. duodeni, C. intest. non-spec.

Age	Cancer recti			Cancer hepatis			Cancer pancreatis			Cancer abdominis			Cancer bili		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	—	—	—	—	1	0.02	—	—	—	1	1	0.04	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	3	—	0.06	—	—	—	—	—	—	—	—	—	—	—	—
20—24	2	—	0.04	1	1	0.04	—	—	—	1	—	0.02	1	—	0.02
25—29	4	—	0.09	1	—	0.02	—	—	—	2	—	0.04	2	—	0.04
30—34	5	—	0.10	1	—	0.02	—	—	—	4	—	0.08	10	—	0.21
35—39	21	—	0.47	3	1	0.09	4	—	0.09	3	—	0.07	20	—	0.45
40—44	40	—	1.00	3	3	0.15	9	—	0.22	2	3	0.12	28	—	0.70
45—49	57	3	1.66	11	1	0.33	14	4	0.50	4	7	0.31	29	—	0.80
50—54	94	5	3.21	13	4	0.55	11	4	0.49	6	6	0.39	43	—	1.39
55—59	122	18	5.07	17	10	0.98	19	8	0.98	12	9	0.76	32	1	1.19
60—64	157	26	7.87	22	14	1.55	28	9	1.59	13	8	0.90	49	—	2.11
65—69	157	42	10.51	21	12	1.74	27	9	1.90	14	20	1.80	36	—	1.90
70—74	130	47	13.72	21	26	3.64	21	10	2.40	22	20	3.26	39	1	3.10
75—79	99	41	17.68	14	28	5.30	14	13	3.41	5	33	4.80	29	—	3.66
80—84	50	28	19.85	2	25	6.87	5	4	2.29	2	26	7.12	18	—	4.58
85—	14	18	18.14	2	9	6.24	—	3	1.70	1	12	7.37	14	—	7.94
Females															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	1	—	0.02	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	2	—	0.04	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	3	0.06	1	—	0.02	—	—	—	—	—	—	—	—	—
25—29	3	2	0.11	1	1	0.04	—	1	0.02	2	—	0.04	1	—	0.02
30—34	12	2	0.29	1	—	0.02	1	—	0.02	2	3	0.10	—	—	—
35—39	21	1	0.48	2	—	0.04	3	—	0.07	3	2	0.11	2	—	0.04
40—44	22	1	0.54	7	2	0.21	6	3	0.21	9	6	0.35	2	—	0.05
45—49	50	5	1.43	14	6	0.52	4	1	0.13	13	11	0.63	3	—	0.08
50—54	63	4	2.03	18	11	0.88	7	3	0.30	10	13	0.70	4	—	0.12
55—59	83	19	3.42	26	19	1.51	20	11	1.04	34	14	1.61	2	3	0.17
60—64	93	14	4.28	36	20	2.24	25	6	1.24	35	29	2.56	4	—	0.16
65—69	73	18	4.51	25	29	2.68	24	14	1.88	31	45	3.77	6	—	0.30
70—74	89	26	7.97	25	55	5.54	28	17	3.12	31	68	6.86	7	—	0.49
75—79	46	37	8.92	14	40	5.81	19	8	2.90	17	84	10.86	—	—	—
80—84	24	20	8.94	11	21	6.50	7	7	2.85	6	52	11.79	—	—	—
85—	4	13	7.41	2	17	8.28	1	7	3.49	1	22	10.02	—	—	—

Age	Cancer tract. respir. et digest. sup.[1]			Cancer pulmonis			Cancer prostatae			Cancer penis			Cancer testis		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	3	—	0.06
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	2	—	0.04	—	—	—	1	—	0.02	—	—	—	—	—	—
15—19	4	—	0.08	1	—	0.02	—	—	—	—	—	—	4	2	0.12
20—24	3	—	0.06	1	—	0.02	—	—	—	—	—	—	12	—	0.24
25—29	—	—	—	—	—	—	1	—	0.02	1	—	0.02	24	2	0.55
30—34	5	1	0.12	8	1	0.18	—	—	—	2	—	0.04	28	2	0.62
35—39	13	1	0.32	16	5	0.47	—	—	—	2	—	0.05	29	2	0.70
40—44	15	1	0.40	31	5	0.90	—	—	—	6	—	0.15	11	—	0.27
45—49	20	—	0.55	49	9	1.61	6	—	0.17	3	—	0.08	12	1	0.36
50—54	29	1	0.97	76	2	2.53	12	3	0.49	9	2	0.36	8	—	0.26
55—59	35	4	1.41	89	25	4.13	41	4	1.63	6	—	0.22	3	1	0.14
60—64	51	7	2.49	69	27	4.13	52	9	2.62	10	—	0.43	3	1	0.17
65—69	65	4	3.64	50	17	3.54	123	31	8.14	12	—	0.63	3	1	0.21
70—74	36	8	3.41	36	27	4.88	136	38	13.49	12	—	0.93	1	1	0.16
75—79	26	1	3.41	16	19	4.42	59	33	11.62	8	2	1.26	1	2	0.38
80—84	20	7	6.87	6	5	2.80	36	20	14.25	6	2	2.04	2	1	0.76
85—	6	6	6.80	—	4	2.27	12	8	11.34	1	1	1.13	—	1	0.57
Females															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	1	—	0.02	—	—	—	—	—	—	—	—	—	—	—	—
15—19	1	—	0.02	—	—	—	—	—	—	—	—	—	—	—	—
20—24	1	—	0.02	1	—	0.02	—	—	—	—	—	—	—	—	—
25—29	2	—	0.04	—	1	0.02	—	—	—	—	—	—	—	—	—
30—34	4	1	0.10	1	3	0.08	—	—	—	—	—	—	—	—	—
35—39	4	1	0.11	5	1	0.13	—	—	—	—	—	—	—	—	—
40—44	10	1	0.26	2	—	0.05	—	—	—	—	—	—	—	—	—
45—49	6	—	0.16	8	5	0.34	—	—	—	—	—	—	—	—	—
50—54	19	5	0.73	13	3	0.49	—	—	—	—	—	—	—	—	—
55—59	18	2	0.67	27	10	1.24	—	—	—	—	—	—	—	—	—
60—64	14	3	0.68	22	8	1.20	—	—	—	—	—	—	—	—	—
65—69	26	3	1.44	29	13	2.08	—	—	—	—	—	—	—	—	—
70—74	33	9	2.91	8	13	1.46	—	—	—	—	—	—	—	—	—
75—79	20	4	2.58	4	17	2.26	—	—	—	—	—	—	—	—	—
80—84	10	7	3.46	1	4	1.02	—	—	—	—	—	—	—	—	—
85—	2	7	3.92	—	4	1.74	—	—	—	—	—	—	—	—	—

[1] C. linguae, mucosae cavi oris, maxillae et mand., tonsillae, pharyngis, laryngis, gl. saliv.

Age	Cancer renis			Cancer vesicae urinar.			Lymfogranulomatosis (Hodgkin)			Leukosis typi incerti, Myelomata etc.			Leukosis myeloica[1]		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
25—29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30—34	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
35—39	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
40—44	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
45—49	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
50—54	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
55—59	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
60—64	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
65—69	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
70—74	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
75—79	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
80—84	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
85—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Females															
0—4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5—9	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
10—14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
15—19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
20—24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
25—29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
30—34	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
35—39	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
40—44	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
45—49	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
50—54	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
55—59	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
60—64	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
65—69	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
70—74	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
75—79	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
80—84	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
85—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

[1] C. linguae, mucosae cavi oris, maxillae et mand., tonsillae, pharyngis, laryngis. gl. saliv.

Age	Cancer renis			Cancer vesicae urinar.			Lymfogranulomatosis (Hodgkin)			Leukosis typi incerti, Myelomata etc.			Leukosis myeloica[1]		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	5	1	0.11	1	—	0.02	1	—	0.02	2	2	0.08	9	1	0.19
5—9	2	—	0.04	—	—	—	1	—	0.02	1	1	0.04	2	—	0.04
10—14	—	—	—	—	—	—	6	—	0.13	1	1	0.04	3	—	0.07
15—19	—	—	—	—	—	—	7	—	0.15	1	—	0.02	2	—	0.04
20—24	—	—	—	—	1	0.02	14	1	0.30	3	2	0.10	7	—	0.14
25—29	1	—	0.02	2	—	0.04	12	—	0.26	1	—	0.02	3	1	0.09
30—34	5	—	0.10	—	1	0.02	15	2	0.35	3	—	0.06	6	2	0.16
35—39	5	—	0.11	6	—	0.14	8	4	0.27	2	2	0.09	6	2	0.18
40—44	4	—	0.10	5	1	0.15	8	1	0.22	2	—	0.05	2	—	0.05
45—49	13	3	0.44	16	2	0.50	5	—	0.14	2	3	0.14	6	—	0.17
50—54	14	5	0.62	30	3	1.07	3	1	0.13	8	1	0.29	6	—	0.19
55—59	16	7	0.83	23	3	0.94	8	—	0.29	10	2	0.43	8	1	0.33
60—64	28	2	1.29	28	7	1.51	3	2	0.22	17	3	0.86	8	—	0.34
65—69	31	7	2.01	41	9	2.64	5	—	0.26	7	3	0.53	6	2	0.42
70—74	14	10	1.86	32	11	3.33	3	—	0.23	5	6	0.85	7	1	0.62
75—79	8	5	1.64	17	15	4.04	4	1	0.63	4	4	1.01	1	1	0.25
80—84	5	4	2.29	11	7	4.58	—	1	0.25	—	1	0.25	—	1	0.25
85—	5	2	3.97	3	8	6.24	—	1	0.57	—	—	—	—	1	0.57
Females															
0—4	1	1	0.04	—	—	—	—	1	0.02	2	4	0.12	4	2	0.12
5—9	—	—	—	—	—	—	1	—	0.02	1	—	0.02	2	—	0.04
10—14	—	—	—	—	—	—	2	1	0.07	—	—	—	1	—	0.02
15—19	—	—	—	—	—	—	2	1	0.06	2	2	0.08	3	—	0.06
20—24	—	—	—	—	1	0.02	7	—	0.14	—	1	0.02	1	—	0.02
25—29	2	—	0.04	—	—	—	16	2	0.38	—	1	0.02	4	—	0.08
30—34	—	—	—	2	—	0.04	20	4	0.49	—	—	—	6	—	0.12
35—39	2	—	0.04	1	—	0.02	7	3	0.22	1	—	0.02	6	—	0.13
40—44	5	3	0.19	4	1	0.12	7	2	0.21	3	—	0.07	6	—	0.14
45—49	9	1	0.26	5	2	0.18	5	3	0.21	—	3	0.08	8	2	0.26
50—54	20	1	0.64	7	1	0.24	5	—	0.15	2	3	0.15	12	—	0.36
55—59	27	4	1.04	9	2	0.37	4	2	0.20	13	3	0.54	12	2	0.47
60—64	24	6	1.20	13	3	0.64	4	2	0.24	9	2	0.44	6	1	0.28
65—69	21	3	1.19	23	7	1.49	5	2	0.35	9	4	0.64	12	3	0.74
70—74	10	7	1.18	19	5	1.66	—	—	—	7	2	0.62	7	—	0.49
75—79	9	5	1.51	10	3	1.40	2	1	0.32	—	4	0.43	3	—	0.32
80—84	6	4	2.03	8	8	3.25	—	—	—	—	3	0.61	—	—	—
85—	—	2	0.87	2	3	2.18	1	—	0.44	—	—	—	—	—	—

[1] acut. et chron.

Age	Leukosis lymphatica[1]			Cancer cerebri			Cancer cutis			Cancer metast.[2]			Cancer alior. organ. et local. incert.		
	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living	Hospital Cases	Death certificates only	All Cases pr 10,000 living
Males															
0—4	10	3	0.25	6	5	0.21	1	1	0.04	—	—	—	11	—	0.21
5—9	3	2	0.11	5	3	0.17	2	—	0.04	—	1	0.02	2	1	0.06
10—14	2	—	0.04	9	1	0.22	1	—	0.02	—	—	—	1	1	0.04
15—19	6	—	0.12	6	2	0.17	—	—	—	—	—	—	2	—	0.04
20—24	5	2	0.14	8	4	0.24	3	—	0.06	1	—	0.02	5	1	0.12
25—29	3	—	0.06	14	3	0.36	12	—	0.26	2	1	0.06	2	—	0.04
30—34	5	—	0.10	13	9	0.45	15	—	0.31	1	—	0.02	8	2	0.21
35—39	3	—	0.07	10	8	0.41	19	—	0.43	6	—	0.14	6	1	0.16
40—44	2	—	0.05	21	9	0.75	39	1	1.00	8	1	0.22	13	1	0.35
45—49	7	1	0.22	17	14	0.86	49	1	1.39	14	1	0.42	13	—	0.36
50—54	20	4	0.78	16	14	0.97	86	1	2.82	16	2	0.58	14	7	0.68
55—59	20	3	0.83	14	17	1.12	86	—	3.11	19	5	0.87	14	6	0.72
60—64	23	4	1.16	11	9	0.86	129	3	5.68	31	11	1.81	23	4	1.16
65—69	30	5	1.85	3	8	0.58	159	5	8.66	22	3	1.32	14	6	1.06
70—74	17	6	1.78	1	3	0.31	149	1	11.63	17	16	2.56	14	8	1.71
75—79	11	2	1.64	—	1	0.13	132	7	17.55	16	6	2.78	10	3	1.64
80—84	4	1	1.27	—	1	0.25	87	7	23.92	2	3	1.27	7	5	3.05
85—	—	—	—	—	—	—	41	13	30.61	—	5	2.83	1	2	1.70
Females															
0—4	8	2	0.20	2	3	0.10	2	—	0.04	—	—	—	7	1	0.16
5—9	1	—	0.02	7	6	0.29	1	—	0.02	—	—	—	—	—	—
10—14	1	—	0.02	4	3	0.16	3	—	0.07	—	—	—	2	—	0.05
15—19	1	—	0.02	3	—	0.06	1	—	0.02	—	1	0.02	2	1	0.06
20—24	1	—	0.02	9	5	0.28	7	—	0.14	—	1	0.02	2	—	0.04
25—29	2	—	0.04	5	3	0.17	8	—	0.17	—	—	—	1	—	0.02
30—34	3	—	0.06	14	1	0.31	14	—	0.29	2	1	0.06	6	1	0.14
35—39	1	1	0.04	7	15	0.48	21	—	0.46	5	3	0.17	15	2	0.37
40—44	1	—	0.02	9	6	0.35	33	—	0.78	9	—	0.21	15	1	0.38
45—49	4	—	0.10	22	7	0.76	61	—	1.59	10	2	0.31	19	2	0.55
50—54	12	2	0.42	16	13	0.88	50	1	1.55	17	—	0.52	15	3	0.55
55—59	17	3	0.67	10	18	0.94	76	1	2.58	17	9	0.87	30	3	1.11
60—64	11	1	0.48	7	11	0.72	87	3	3.60	31	8	1.56	20	10	1.20
65—69	13	2	0.74	6	7	0.64	104	2	5.26	16	7	1.14	13	10	1.14
70—74	7	1	0.55	1	3	0.28	124	3	8.80	18	5	1.59	18	9	1.87
75—79	2	2	0.43	—	1	0.11	88	5	10.00	14	8	2.37	13	14	2.90
80—84	2	1	0.61	—	—	—	62	6	13.82	3	5	1.63	9	5	2.85
85—	2	—	0.87	—	—	—	40	8	20.92	2	2	1.74	5	5	4.36

[1] acut. et chron. — [2] incl. C. metast. pulm., C. metast. hepat., C. metast. lymphonod.

SUMMARY

Number of cases notified to The Danish Cancer Registry 1942—44 for several frequent sites, distributed on age, separately for cases notified through hospitals and cases known by death certificates only.

ZUSAMMENFASSUNG

Bericht über die dem Dänischen Krebsverzeichnis 1942—44 gemeldeten Fälle nach ihrer Verteilung auf verschiedene, häufige Lokalisationen und verschiedene Altersklassen. Die aus Krankenhäusern gemeldeten Fälle und die nur durch die Totenscheine bekannten sind gesondert aufgeführt.

RÉSUMÉ

Nombre des cas annoncés à l'Enregistrement Danois du Cancer de 1942 à 1944, de diverses localisations fréquentes, avec répartition par classes d'âge, différence faite entre ceux provenant des hôpitaux, et ceux n'étant connus que par les certificats de décès.

... acut. et chron. — ... incl. C. metast. pulm., C. metast. hepat., C. metast. lymphonod.

AUS DER RÖNTGEN-ABTEILUNG DES ZENTRALLAZARETTES, GÄVLE, SCHWEDEN
(CHEF: LASARETTSLÄKARE DR. SIGFRID ARNELL)

CONJUNKTIVAL- UND CUTAN-TEST BEI VERWENDUNG VON JOD-KOMPLEXSALZEN ALS RÖNTGEN-KONTRASTMITTEL[1]

von

Gustaf Notter

In Anlehnung an die Arbeiten von ROBINS (1) und ARCHER (2) wurden an der hiesigen Rtg.-Abteilung 100 Patienten vor der iv. Injektion des Kontrastmittels mit 2 Vorproben gleichzeitig untersucht. Zur Anwendung kamen die komplexen Jodsalzverbindungen: Joduron (Cilag) 30 %, Umbradil (Astra) 35 % und Kontrast »U» (Leo) 20 %. Die teils klinischen, teils ambulanten Patienten wurden folgenden Rtg.-Untersuchungen unterzogen: Iv. Urographie, Artrographie und Myelographie. Das Durchschnittsalter lag bei 44, bei Patienten im Alter von 1—74 Jahren. Beide Geschlechter waren ungefähr gleichstark vertreten.

Die *intracutane* Probe wird mit 0.1 ccm unverdünnter Lösung auf dem Oberschenkel ausgeführt, um bei der Stauung am Arm zur iv. Inj. nicht eine pos. Reaktion zu zerstören. Die gesetzte Quaddel misst 3—4 mm im Durchmesser. 15 Min. nach der Injektion wird der Durchmesser der Quaddel und des umgebenden Erythems gemessen und in cm angegeben.

Quaddeln über 1 cm werden als stark positiv bezeichnet.

Erythem bis 2 × 2 cm als schwach und negativ,
von 2 × 2 cm bis 4 × 4 cm als normal positiv,
von 4 × 4 cm bis 7 × 7 cm und grösser als stark positiv bezeichnet.

Oedem, *Urticaria* usw. gelten als besonders stark positiv.

Die *conjunktivale* Probe wird nach Kontrolle *beider* Augen (zum Ausschluss einer ev. vorliegenden einseitigen oder doppelseitigen Entzündung oder Erkrankung) an *einem* Auge so ausgeführt, dass man 2 Tropfen unverdünnter Lösung in den Conjunktivalsack einträufelt.

[1] Bei der Red. am 31. XII. 1948 eingegangen.

Dann schliesst der Pat. die Augen. Die Beurteilung erfolgt nach 3. Min. Entzündete oder erkrankte Augen scheiden für die Methode aus.

ARCHER (2) gibt 3 Grade für die positive Beurteilung an.

1) Minimale conjunktivale Injektion.

2) Mässige conjunktivale und leichte ciliare Injektion. Dabei oft Nausea, Vomitus, Pruritus, Urticaria und Oedem.

3) Starke ciliare Injektion von der Iris bis zur Peripherie. Absolute Kontraindikation zur Kontrastmittelinjektion: Drohender Vasomotoren-Kollaps, Larynxoedem, Asthma, Urticaria und Dermatitis.

Beim Einträufeln der Lösung verspürt man ein sofort einsetzendes Brennen im Conjunktivalsack, das mit steigender Konzentration des Jodsalzes zunimmt. Beim 20 %igen Kontrast »U» ist es nur mässig, während man es beim 50 %igen Umbradil kaum erträgt. Die 35 %ige Lösung, die ja bei der iv. Urographie gewöhnlich zur Anwendung kommt, wird aber von den meisten Pat. gut vertragen. Man muss den Pat. vor dem Einträufeln nur auf dieses, ungefähr $^1/_2$ Min. anhaltende Brennen aufmerksam machen und ihn bitten, jedes Reiben des Auges zu vermeiden. Die Pipette oder Kanüle darf ausserdem nicht mit Alkohol ausgespült sein!

Alle aufgeführten Jodverbindungen wurden bei den Testproben gleichgut vertragen. Jeder Pat. wurde nach dem folgenden Schema, das dem von ROBINS (1) angegebenen weitgehend gleicht, befragt und untersucht.

Schema: .....

Name: ..... Alter: ..... Datum: ..... Abteilung: .....
Allergische Familienanamnese: Asthma, Heuschnupfen, Ekzem, Nesselfieber usw.
Eigene Anamnese: .....
Vorangegangene Jodkontrastuntersuchung. B. Urographie usw.: .....
Wurde diese Untersuchung gut vertragen? .....
Andere Jodmedikation? ..... Struma? .....
Heute angewandtes Präparat: ..... Konzentration? ..... ccm? .....

Test: .... *intracutan:* ..... nach 15 Min.!
Hautsymptome: Oedem, Erythem, Quaddel (Durchmesser in cm)
conjunktival: ..... nach 3 Min.!
conjunktivale oder ciliare Injektion? .....

Nach Injektion des gesamten Kontrastes:

Hautsymptome: .....
Conjunktivalsymptome: .....
Allgemeine Symptome: Husten, Schnupfen, Niessen, Kurzatmigkeit, Erbrechen, Schwindel, Ohnmacht.
Nach wieviel Min. traten Symptome auf? .....
Länge des Anfalls? .....
Erfolg auf Adrenalintherapie? .....

In 15 Fällen war eine Urographie, in 4 Fällen eine Myeolographie vorausgegangen. 6 Patienten hatten eine Struma und hatten Jodpräparate erhalten. Diese Jodmedikation darf jedoch nicht überschätzt werden, da bei dem weitverbreiteten Gebrauch von jodhaltigem Speisesalz fast jeder Pat. in Schweden mit Jod »sensibilisiert» ist. 26 Patienten wiesen eine allergische Familien- oder eigene Anamnese auf. Von diesen hatten 9 Pat. = 38.5 % gesteigerte Haut- und Allgemein-Symptome, während von den nicht »belasteten» 74 Pat. 28.4 % die gleichen Symptome aufwiesen.

Das von ROBINS angegebene Schema der Symptombewertung wurde beibehalten.

I. *Normal:* 90 Pat.

48 = 53.3 % normale pos. Reaktion bis 4 × 4 cm
17 = 18.8 % verstärkte pos. Reakt. bis 7 × 7 cm
25 = 27.9 % keine oder sehr schwache Reakt. bis 2 × 2 cm. } *Haut.*

65 = 72.2 % pos. normale Reaktion
15 = 16.7 % stark pos. Reakt.
10 = 11.1 % keine Reaktion } *Conjunktiva.*

II. *Psychogen:* 2 Pat. Im 1. Falle normale Haut- und Conjunktivalprobe
Im 2. Falle Haut neg., Conj. pos.
(Symptome: Rastlosigkeit, Ängstlichkeit, leichte Ohnmacht, Zittern, Schwindel. Keine medikamentöse Behandlung notwendig.)

III. *Neurovasculär:* 1 Pat. Haut und Conj.-Probe neg.
(Symptome: Rotes Gesicht, dann Blässe, Schweiss, Cyanose, weite Pupillen. Tachycardie, kalte Extremitäten. Nausea, Vomitus. Kurze Zeit nach der inj. Teils schwere Symtome, die mit Adrenalin nicht zu beheben sind.)

IV. *Allergisch:* 6 Pat.

4 Pat. normalpositiv.
1 Pat. sehr stark pos. } *Haut-* und *Conjunktival*symptome übereinstimmend.
1 Pat. negativ.

(Symptome: Husten, Schnupfen, Rhinitis, Urticaria, Conjunktivitis, Erbrechen, Gesichts- und Larynx-oedem.

V. *Andere Ursachen* zu Allgemeinerscheinungen sind:

1) Zu schnelle Inj. des Kontrastmittels:
Während normalweise nach 4 ccm ein Wärmegefühl in Brust, Gesicht und Extremitäten (Sympaticuswirkung auf das Stammhirn) und ein leichter Jodgeschmack verspürt wird, kann sehr schnell Übelkeit, Erbrechen und Ohnmacht hinzukommen. Die Injektionsdauer muss daher individualisiert werden, soll aber mindestens 3 Min. betragen.

2) Zu hart liegende Kompression während der Urographie.
Dadurch Kompression der Vena cava und der Bauchplexus. Pat. bekommt blaue Beine, schwitzt, wird unruhig, langsamer Puls, droht zu kollabieren.

Die vergleichende Untersuchung zeigt, dass

33.3 % Pat. mit Allgemeinerscheinungen keinen pos. Test haben und
27.8 % Pat. mit pos. Test keine Allgemeinerscheinungen haben!

Die vergleichenden Zahlen bei ROBINS sind 30 % und 24 %!

Conjunktivale und cutane Probe stimmen nicht immer überein, lassen oft einander im Stich oder zeigen graduelle Unterschiede. Ich kann mich nach meinen Untersuchungen, die zahlenmässig zwar klein sind, aber über die Methode doch einen Überblick gestatten, nicht der Auffassung ARCHERS anschliessen, dass der Ocular-test dem Cutanen überlegen sein soll.

Ausgehend von der Überlegung, dass die empfindliche Conjunktiva des Auges auf jede hypertonische Lösung mit einer Gefässreaktion antworten muss, die in ihrer Stärke und ihrem Verlauf ganz von der Konzentration der Salzlösung abhängig ist (Rickersches Stufengesetz), halte ich daher nicht einmal für bewiesen, dass die conjunktivale Reaktion eine »hyperergische» ist. Ich halte sie vielmehr für eine durch hypertonischen Reiz verursachte Nerven- und Gefässirritation, die zu einer unmittelbaren Schliessung des Auges, vermehrten Tränenfluss und einer langsam abnehmenden Hyperämie in Conjunktival- und Ciliar-Gefässen führt.

Alle Proben, sowohl die conjunktivale, wie auch die intra-, sub-cutane und die von anderer Seite empfohlene linguale Methode haben eine zu grosse Fehlerbreite (bis zu 33.3 %), um eine von ihnen als absolut zuverlässig bezeichnen zu können.

In einem Falle machte z. B. ein Pat. mich darauf aufmerksam, dass er jodempfindlich sei. Ich führte daher Proben mit verschiedenen Präparaten und mit besonderem Interesse durch. Das Ergebnis war absolut normal und deutete in nichts auf eine Hyperergie hin. 10 Min. nach der Injektion von 20 ccm i. v. bekam der Pat. regelrechte mittelschwere allergische Symptome mit Luftknappheit, Quaddelbildung über den ganzen Stamm, Erythem, Erbrechen nebst zahlreichen Petechien. Auf Ephedrininjektion baldige Besserung.

Zum Glück sind die wirklich schweren Allergiefälle mit Todesgefahr verhältnismässig gering, sodass wir über die Unverlässigkeit unserer Testmethoden nicht zu verzweifeln brauchen. Auch steht uns als die zuverlässigste Testmethode ja die intravenöse noch zur Verfügung.

Bei der Durchführung einer dieser Testmethoden und deren negativem Ausfall müssen wir uns aber immer der Möglichkeit eines trotzdem auftretenden allergischen Zustandes bewusst sein.

ZUSAMMENFASSUNG

Der Autor untersuchte 100 Patienten mit Conjunktival- und Intracutan-Test bei Urographien, Artrographien und Myelographien mit wasserlöslichen Jod-Komplexsalzen. Beide Teste zeigten grosse Fehlerbreiten und Unzuverlässigkeit. Der Conjunktivaltest wird als zweifelhaft angesehen und ist dem intracutanen nicht überlegen.

SUMMARY

Ophtalmic and intradermal tests were made on 100 patients after urography, arthrography, and myelography using iodides which are soluble in water, as contrast media. These examinations have shown that there is a wide range of error and that the tests are unreliable. The diagnostic value of the ophtalmic test is questioned. It was found that this test is not superior to the intradermal test.

RÉSUMÉ

L'auteur a examiné 100 malades par des tests, soit conjonctivaux, soit intradermiques, lors d'urographies, d'arthrographies et de myélographies pratiquées avec des sels combinés à base d'iode. Ces genres de tests présentent l'un et l'autre une grosse marge d'erreur et aucun des deux n'est digne de confiance. Le test conjonctival est considéré comme douteux et n'est pas supérieur à l'intradermique.

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FROM THE GYNECOLOGICAL DEPARTMENT (CHIEF: DR. H. L. KOTTMEIER) AND FROM THE RADIO-PATHOLOGICAL INSTITUTE (CHIEF: PROF. O. REUTERWALL) OF THE RADIUMHEMMET, STOCKHOLM, SWEDEN

DOUBTFUL MALIGNANT CHANGES IN THE ENDOMETRIAL EPITHELIUM[1]

A report on 60 cases from the Radiumhemmet

by

Gilberto Marrubini

All cases of carcinoma of the uterine body which are referred to the Radiumhemmet are classified according to their microscopic structure, and in accordance with the scheme proposed by REUTERWALL. This classification is drawn in order to establish a possible relationship between the histological structure and the radiosensitivity of the tumour. The adenocarcinomas are divided into six groups, and the tumours with solid structure into two groups, according to the presence or the absence of squamous epithelial metaplasia. The mixed tumours form a separate group. Finally there is a group of »debatable cases» which are markedly suspicious but not characteristic of malignant changes.

For the particulars of this classification the reader is referred to the paper by HEYMAN, REUTERWALL & BENNER (11).

The purpose of this paper is to study the last-mentioned group of cases which offers interesting pecularities both from the clinical and from the pathological standpoints.

In the study of these cases are encountered two different problems the solution of which depends on the experience and on the subjective judgement of the pathologist. The first is to establish the borderline between lesions of obviously benign and those of obviously malignant nature. The second is the determination of the type of changes. Even expert pathologists would, no doubt, disagree on the interpretation of some of these cases. It is probable that this group of cases which is presumably present in every series, is partly responsible for the variation in rates of cure presented by different authors.

[1] Submitted for publication, Dec. 30, 1948.

Few authors have commented on this aspect and the published cases are scanty. HINTZE (1929) reported 24 cases of atypical glandular hyperplasia of the endometrium simulating adenocarcinoma, but which he, nevertheless, considered to be benign. HINTZE claims that his histological diagnosis of benignancy was confirmed by the follow-up study of the patients, since none later developed cancer. However, since the longest follow-up period was 2 and 3/4 years only, the statement must be accepted with reserve.

TAYLOR (1932) in a series of 85 cases of endometrial hyperplasia, 152 cases of carcinoma of the uterine body, and 128 »cases incorrectly diagnosed as hyperplasia», found 6 cases »which had many of the features of carcinoma», which, however, could not be definitely diagnosed as cancer.

NOVAK & RUTLEDGE (1948) reported 44 instances of »atypical glandular hyperplasia simulating adenocarcinoma». They pointed out that lesions of this nature frequently present a problem even to the expert pathologist. In 18 of the cases they concluded that the changes did not warrant radical treatment. In some of the remaining 26 cases they believed that the changes were probably benign, but nevertheless, required radical treatment. A possible malignancy could not be excluded in the remainder. The microscopic diagnosis of a benign nature of the lesion was confirmed by the follow-up, since none of the patients developed an endometrial cancer in the years following the treatment. It is worth mentioning that in many cases the treatment was limited to curettage.

In the Radiumhemmet series (1914 to 1943 inclusive) there are 1,014 cases registered as cancer of the uterine body. Of these, 65 instances were allotted to the group of »debatable cases» according to the aforementioned classification of REUTERWALL. After thorough revision it was found necessary to exclude for different reasons ten of the cases from the material. The main reason was that the amount of tissue available was insufficient to permit an assessment of the general structure of the endometrium. Four cases were excluded on these grounds. In three additional cases the epithelial changes were sufficiently marked to justify the diagnosis of definite cancer. Finally, three cases had to be excluded since the epithelial changes were not sufficiently marked to justify their inclusion among the »debatable cases». On the other hand five cases were added to the group: the histological study of the endometrium revealed epithelial changes of the same type as in the other patients. Four of these were registered as ovarian tumours. The fifth case was classified as a »cancer corporis et colli uteri» (according to the clinical classification of HEYMAN). Thus the complete material consists of 60 cases.

These »debatable cases» are borderline-cases between the benign and the malignant, similar, from a general pathological standpoint, to tho e

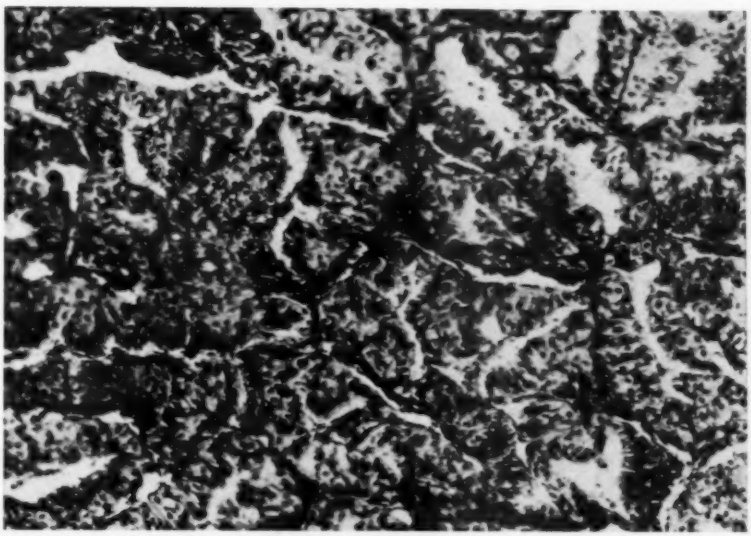

Fig. 1 — 5012/42 — Group 1 (writer's classification v. page 4), × 125.

borderline-cases which may be observed, for instance, in the breast, in the ovaries, and in the salivary glands. It is impossible to consider these lesions as precancerous, according to the concept of NOVAK & YUI, *i. e.* »as indicating a lesion which predisposes to cancer». In fact, in many instances the changes are so marked as to arouse the suspicion that an adenocarcinoma is probably already present, even if it is impossible to demonstrate it. It is also impossible to define these changes as »stages of transition» towards a cancer, along the lines accepted for some lesions of the cervix (so called intra-epithelial cancer). It is not in fact known if these lesions of the endometrium, not radically treated, would develop into definite cancer or not.

It would be of great value in a study of this kind to have a control group of cases showing the same endometrial changes, which have not been radically treated, so as to enable us to compare the evolution of the treated and the untreated cases. But, as NOVAK & RUTLEDGE pointed out, very few gynaecologists would have the courage not to treat patients with such suspicious lesions radically. This is the reason why there are no such untreated or conservatively treated cases in the Radiumhemmet series.

The strong suspicion of malignancy, both from the pathologic and from the clinical standpoints, was in every case an indication for the line

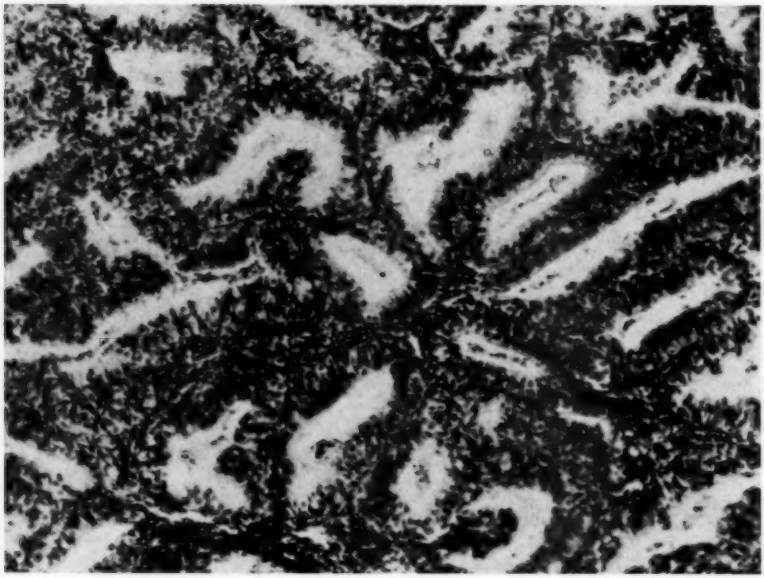

Fig. 2 — 5012/42 — Group 1, × 125.

of therapy adopted, *i. e.* that used for cases of histologically proved cancer. From this fact two different questions naturally arise: 1) was the adopted therapeutic criterion justified? and 2) were these, in the light of their subsequent histories, really cases of carcinoma, although histologically ambiguous?

Only the follow-up study of the patients can give an answer to these questions.

The Material

Pathology

For the histological examination the material has been divided, according to the microscopical features, into 3 groups, as follows:

1) cases in which there are suspicious changes in a functioning endometrium, frequently with more or less typical glandular-cystic hyperplasia of the Swiss-cheese type,

2) cases showing a very marked glandular proliferation in an non-functioning endometrium,

3) cases in which the changes suspicious of malignancy are found in an endometrial polyp.

Fig. 3 — 975/26 — Group 2, × 125.

This classification will enable us to establish the relative incidence of each histological feature in all the material.

With the terms »functioning» and »non-functioning» endometrium, the writer implies the presence or the absence of the classical cyclic changes, both proliferation and secretion, as observed in the endometrium of the reproductive period. It is obviously very difficult to decide in every case whether the endometrium is of functioning or non-functioning type. It is therefore stressed that the criterion for grouping the cases under group 1 or group 2 was the general aspect of the endometrium in which the atypical growth was observed. This distinction was not made in cases in which the lesions suspicious of malignancy occurred in obvious endometrial polyps (group 3).

The 60 cases recorded here are distributed as follows:

Table 1

Group	Number of cases
1	24
2	18
3	18

It should be stressed that most of the cases have common histological features, but differ in detail. Thus, in the first and second groups the lesions

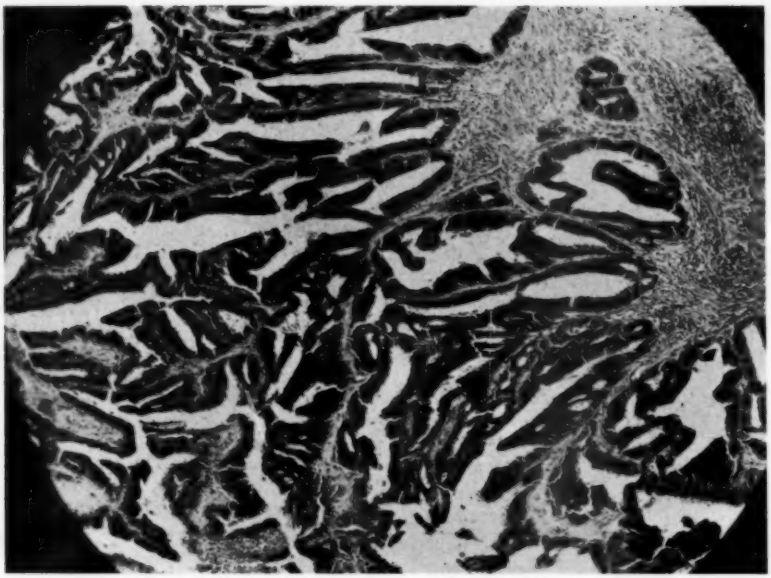

Fig. 4 — 975/26 — Adenocarcinoma developed $3^1/_2$ years after the primary lesion as in fig. 3.

are, from a general pathological standpoint, all hyperplastic in nature. Some, however, approach the typical Swiss-cheese form of hyperplasia, while others show merely an increase in the number of glands.

Cases with a functioning endometrium have been classified under a separate group, since out of 24 cases with hyperplastic changes in a functioning endometrium, 17 occurred in the menopause. In four of the remaining patients, who had long passed the menopause, granulosa-cell tumours were doubtless responsible for the functioning aspect of the mucosa if not for the carcinoma-like epithelial changes. The remaining three patients who had respectively passed the menopause 28, 19 and 9 years previously, showed a functioning endometrium: it is therefore very likely that there was a coexisting functioning ovarian tumour, even if it could not be revealed by the clinical examination. It must moreover be pointed out that, according to the records these patients, as well as the others in group 1, were not given oestrogenic hormones.

In all the cases investigated, changes occurred solely in glands and glandular epithelium. The most atypical features were observed mainly in the cases classified under group 2.

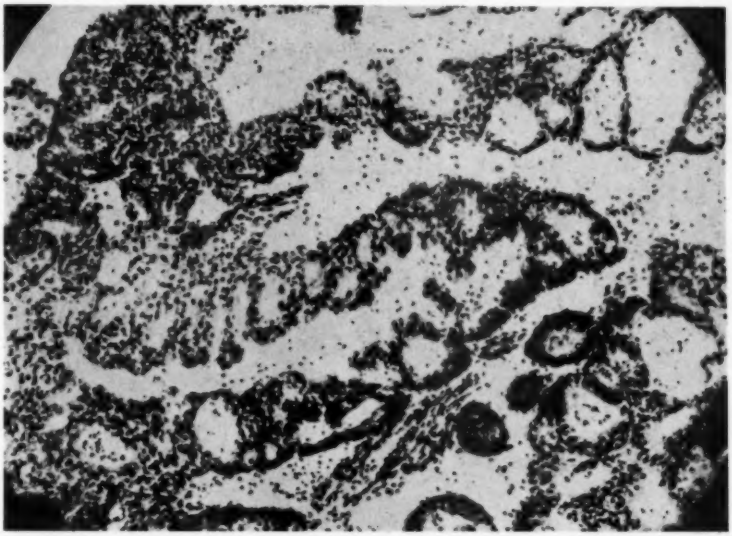

Fig. 5 — 607/23 — Group 2, × 130.

The glands were very frequently increased in number, sometimes enormously so, and were often so closely packed as to resemble the structure of a highly organized adenocarcinoma (v. Fig. 1, 2, 11, 14). Great differences were observed in their shape and size: cystic changes were noted in some of these cases, as well as irregular packing of convoluted glands (v. Fig. 12).

Everywhere more or less marked irregularities of the glandular epithelium could be seen: frequently there was stratification of cells into two or more layers, sometimes locally, sometimes diffusely. The nuclei of these cells lay on different levels and in many instances abundant mitoses were found. There were frequent differences in the staining of the epithelia, some of which were darkly stained, others very slightly. Papillary projections into the glandular lumina were also observed and here and there the formation of secondary lumina in the epithelium. There were often islands of squamous epithelial metaplasia (v. Fig. 9), but, as is well-known, this feature *per se* does not indicate malignancy. These metaplastic areas were at times observed in the glandular epithelium, at others in the surface epithelium.

The stroma was in some zones very scanty, elsewhere it was more abundant, but in no case dit it show changes which would arouse suspicion of a sarcomatous growth. All the aforementioned changes were

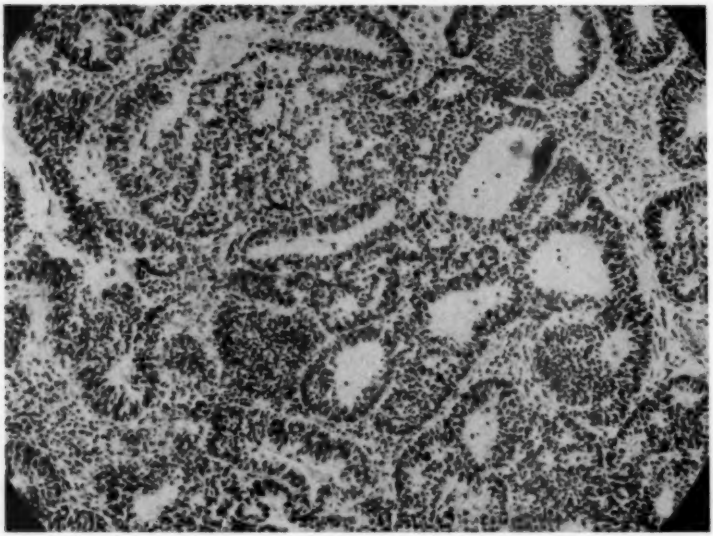

Fig. 6 — 720/22 — Group 2, × 130.

also found to be especially marked in the cases of endometrial polyps (v. Fig. 12, 13, 14). It has been suggested by NOVAK & YUI that when such atypical features are observed in polyps of the uterine body they must be considered to be less suspicious of malignancy than when they are found in the endometrium proper.

This suspicion nevertheless remains. How far it is justified is shown by the fact that three of six patients recorded here who developed carcinoma after radium treatment of the primary endometrial lesion, originally showed uterine polyps with the above mentioned changes (v. Table 3). The problem of the potential malignancy of endometrial polyps is not within the scope of the present paper: this has been discussed by KOTTMEIER (20).

Among the 16 cases in group 2, five showed a few small areas in which a functioning endometrium was suspected, and in one case there were areas of squamous epithelial metaplasia. Two cases in group 3 presented some areas of glandular-cystic hyperplasia, while in four cases zones of more or less marked squamous epithelial metaplasia could be seen. In 4 cases of the 24 belonging to group 1, a marked glandular-cystic hyperplasia was observed: in one case the irregularities of the glands were in some areas so marked as to resemble those observed in the cases under group 2.

In six cases it could not be stated definitely that the lesions were not situated in a polyp even if the diagnosis of polyp could not definitely be made. Areas of squamous epithelial metaplasia were observed in one case.

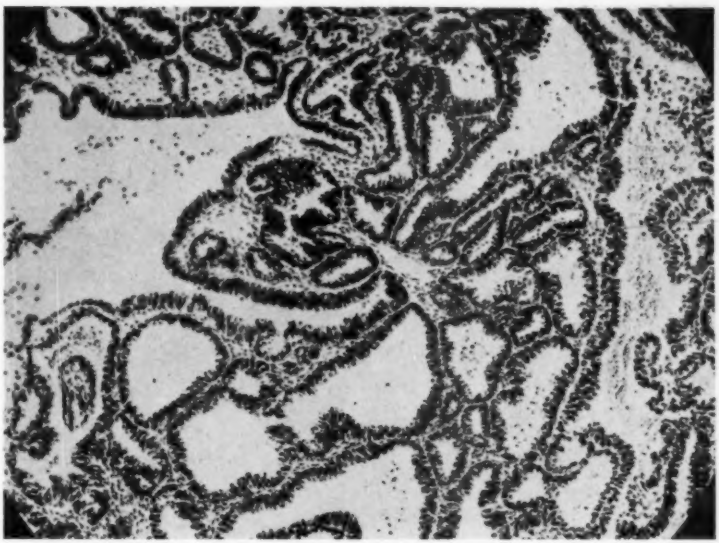

Fig. 7 — 577/20 — Group 2, × 130.

The most important general reasons why a definite diagnosis of adenocarcinoma could not be established in the foregoing cases are: 1) the epithelial changes were always confined to the glands without any obvious destruction of the membrana propria. 2) the different types of changes which have been described did not all occur in the same case. For example, in some instances, although the packing of the glands was strongly suspicious, the epithelium showed no obvious atypical changes. In others the glands were rather regularly distributed, whereas their epithelium showed a marked pleomorphism or abundant intraglandular vegetations.

Clinical features:

The age distribution of the patients was as follows:

Table 2

Age in years	Number of cases
<35	1
35—45	7
45—55	28
55—65	14
65—75	10

Twenty-nine of these patients had passed the menopause at least one year before the endometrial lesion was diagnosed, 20 were menopausal and 11 in the reproductive period.

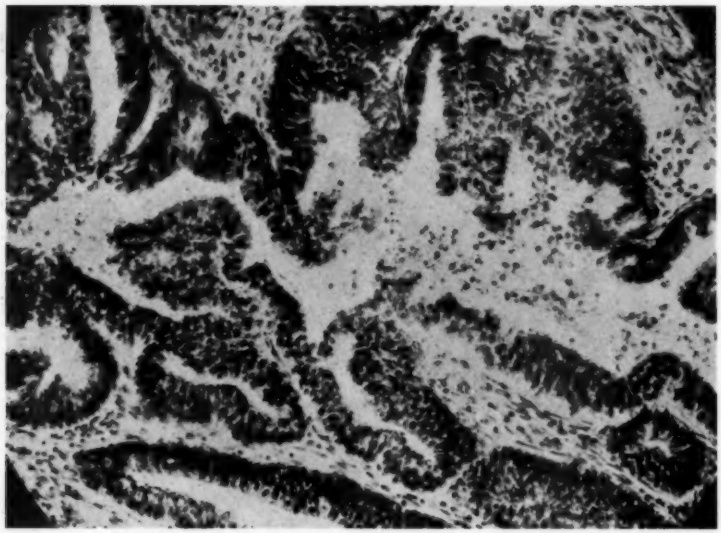

Fig. 8 — 608/21 — Group 2, × 130.

The symptomatology of the patients was usually limited to irregular bleedings of varying duration. In the post-menopausal patients these irregular bleedings were a far more suspicious symptom of uterine neoplasm then in the patients who were in the menopausal period. Less suspicious, clinically, of malignancy were the 11 patients still in their reproductive period, especially the two under 40.

All the patients were treated by the Stockholm radium technique, in doses ranging from a maximum of 4,370 mg.h. to a minimum of 2,150 mg.h.

Until 1934 a single applicator was used in intrauterine treatment, later on the packing method was applied. For particulars of the treatment the reader is referred to the paper by HEYMAN, REUTERWALL & BENNER (11). All the patients were followed up during a period of at least 5 years: in the first 3 years after treatment they were examined on an average three times a year, and subsequently twice and once a year. A diagnostic curettage was performed whenever repeated haemorrhage or an increase in size of the uterus aroused suspicion of »recurrence».

Forty-nine patients were alive for a period of 4 to 21 years after treatment without any symptom from the genital organs. Only in one case was there a suspicion of cancer, due to a haemorrhage 9 years after the radium treatment. The clinical suspicion was not, however, confirmed by

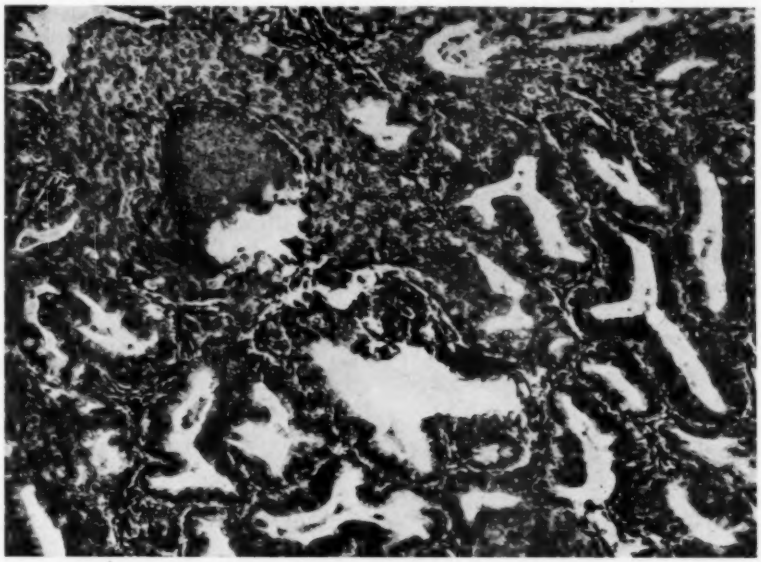

Fig. 9 — 17646/43 — Group 2, × 125.

the histological examination of the curettings which was completely negative.

Seventeen patients died from intercurrent disease (cerebro-vascular accidents, pneumonia etc.). In only one case was it impossible to ascertain the cause of death; her physician suggested the possibility of a cancer of the uterus since she developed ascites which he considered due to abdominal metastases of the primary uterine »cancer». One case must be excluded from the follow-up study since the patient died in diabetic coma the day following the second application of radium. In none of the cases reported was a post-mortem performed.

The other 43 patients are alive and free from evidence of the disease for which they were treated. Two of them were operated on 12 and 2 years after the treatment respectively, the former for a bilateral papilliferous cystadenoma of the ovary and the latter for a right papilliferous ovarian cystoma which were not noticed at the first examination. Both these tumours were benign. It is impossible to establish a relationship between these two benign ovarian tumours and the primary endometrial changes, even if their existence at that period, however improbable, cannot be definitely excluded.

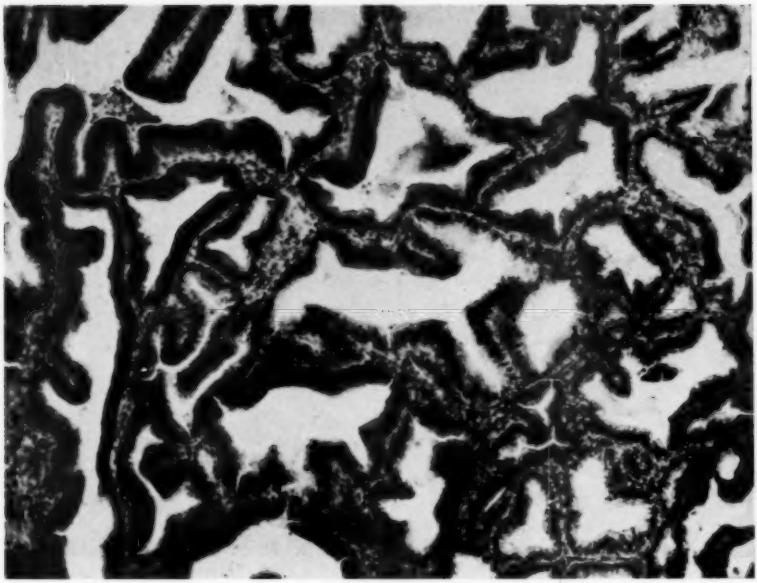

Fig. 10 — 9817/42 — Group 2, × 125.

Among the patients cured of the primary uterine disease, there are two patients one of whom developed a carcinoma of the lower third of the oesophagus, 9 years after the treatment of the uterine disease, the second, a sarcoma of the endometrium 7 years after the same treatment. In the first of these cases a relationship between the carcinoma of the oesophagus and the endometrial changes must be excluded owing to the definite dissimilarity of the histological findings. (The tumour of the oesophagus was a squamous-cell cancer with some cornification.) In the second case it is difficult to correlate the first endometrial lesion, strictly confined to the glandular epithelium without any suspicious changes in the stroma, with the second one, strictly confined to the stroma.

Of the 60 cases recorded here, six developed a cancer within a period of 3 $^1/_2$ to 14 years after the radium treatment of the primary endometrial lesion. In five of these patients the cancer was situated in the endometrium. One was a highly organized and differentiated adenocarcinoma of the adenoma malignum type (group 2 in REUTERWALL's classification), one a highly organized and differentiated adenocarcinoma (group 3), two were less highly organized and differentiated adenocarcinoma up to one-third solid (group 4), and one an adenocarcinoma with squamous epi-

thelial areas (group 5). The sixth patient developed a highly differentiated adenocarcinoma of the right Fallopian tube.

In the last case two possibilities should be considered: 1) the cancer of the tube was already present at the time at which the endometrial lesion was diagnosed this being only a reaction of the endometrium to the tubal carcinoma, 2) the primary endometrial lesion was really malignant and, in spite of the radium treatment, it metastasized to the tube. The last hypothesis appears to be the most feasible, although the microscopic examination of the endometrium of the extirpated uterus showed only post-irradiation, regressive changes.

Table 3 shows the characteristics of these 6 cases.

Table 3

No.	Case	Age in yrs.	Histol. type of the primary lesion (writer's classification) (v. page 4)	Histol. type of recurrent lesion (Reuterwall's classification)	Time of recurrence after treatment	Therapy	Follow-up study
1	E. J. 420/18	56	group 3 (Fig. 13)	adenocarcinoma group 4	14 years	roentgen treatment (inop. because of age)	died 16 years after the primary lesion
2	G. H. 975/26	66	group 2 (Fig. 3)	adenocarcinoma group 4 (Fig. 4)	3½ »	supravaginal amputation (total hysterectomy impossible)	died from heart-failure during convalescence
3	D. O. 2467/32	50	group 2	adenocarcinoma group 2	3½ »	supravaginal amputation removal of adnexa	alive and well
4	N. S. A. 4279/33	65	group 3 (Fig. 12, 14)	adenocarcinoma group 5	9 »	Ra + roentgen treatment (inop. because of age)	died 11 years after the primary lesion from heart disease
5	G. G. M. 5012/42	49	group 1 (Fig. 12)	highly differentiated adenocarcinoma of the right tube	4½ »	total hysterectomy with removal of adnexa	alive and well
6	W. S. E. 7264/42	57	group 3	adenocarcinoma group 3	5 »	total hysterectomy with removal of adnexa	alive and well

All these six patients were given a full radiation dose. In one case, in fact, the highest dose of radium (4,370 mg.h.) in the series had been given.

Attention should, however, be drawn to the different methods of treatment employed. When introducing one or two small irradiators only

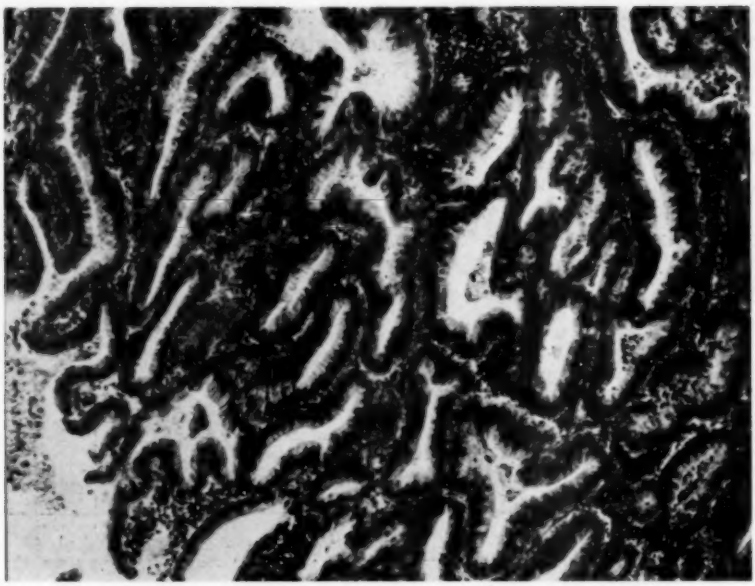

Fig. 11 — 12204/43 — Group 2, × 125.

the irradiation of the uterine wall may be less homogeneous than in the irradiation when the »packing method» is used, particularly in case of a large uterine cavity. A lesion situated in the upper area of the fundus or in the tubal corners may not get an adequate dose if the old technique is used, since it is possible that the irradiator had slipped down to the lower and middle part of the body. Of the six aforementioned cases four were treated according to the old technique and two according to the »packing method». Consequently the »recurrence» cannot be due to inadequate treatment in all cases.

In a group of four patients who showed a functioning endometrium with very suspicious hyperplastic changes, a granulosa-cell-tumour was found. In addition there is one patient with a malignant papilliferous adenocystoma and concomitant endometrial changes. Three of the patients were treated at the Radiumhemmet since the onset of the disease, while two were operated on at other hospitals and referred to the Radiumhemmet for postoperative treatment. The slides of the curettage and the operative specimens are however available in both cases.

In none of the three cases which were diagnosed and treated at the Radiumhemmet was an ovarian tumour noticed at the time of the first

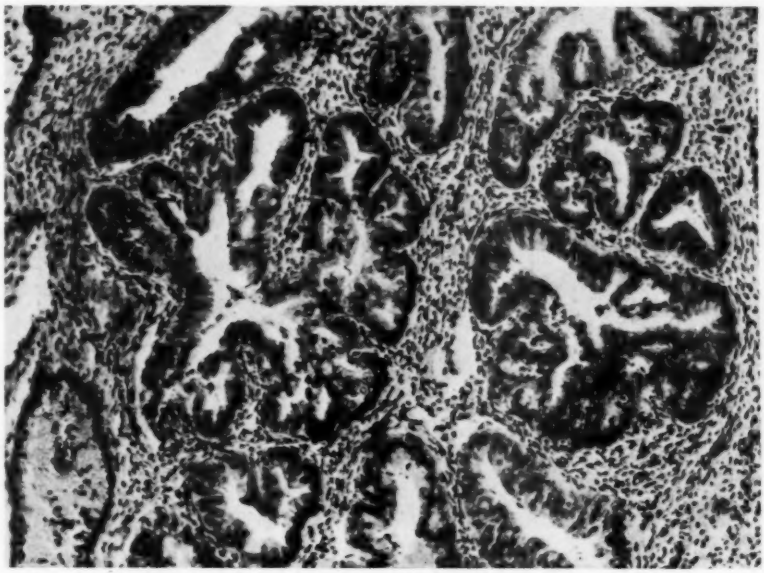

Fig. 12 — 4279/33 — Group 3, × 125.

haemorrhage. Owing to the suspicion of malignancy aroused by the histological examination, the patients were treated with radium in the doses commonly used for cancer. These three patients developed new haemorrhages six months, 3 1/2 years and 3 years respectively after treatment, and only at that time was the ovarian tumour palpable. One of these patients (J. H. A. 1752/33) underwent a bilateral salpingo-oophorectomy. At operation a granulosa-cell tumour with cylindroid structures was found. The patient is still alive and well. The second patient (B. K. I. N. 3301/39) also underwent a bilateral salpingo-oophorectomy, but 3 1/2 years after the operation a mass, the size of a fist, was found in the lower abdomen. She was therefore operated upon again: a tumour of the colon descendens was found and removed by resection. A microscopic examination of the operative specimen revealed a tumour of the same structure as the ovarian tumour removed 3 1/2 years earlier (granulosa cell-tumour with cylindroid structures). One and a half years later a new tumour mass was found in the right iliac fossa: the patient was not operated on again, since this tumour gave rise to no subjective symptom. She is still alive and well. The third patient (W. M. 12165/42) was treated by total hysterectomy and bilateral salpingo-oophorectomy. At operation

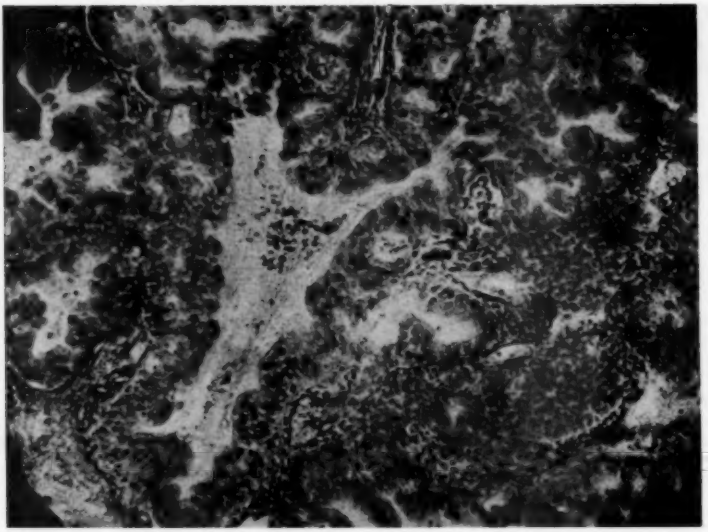

Fig. 13 — 420/18 — Group 3, × 130.

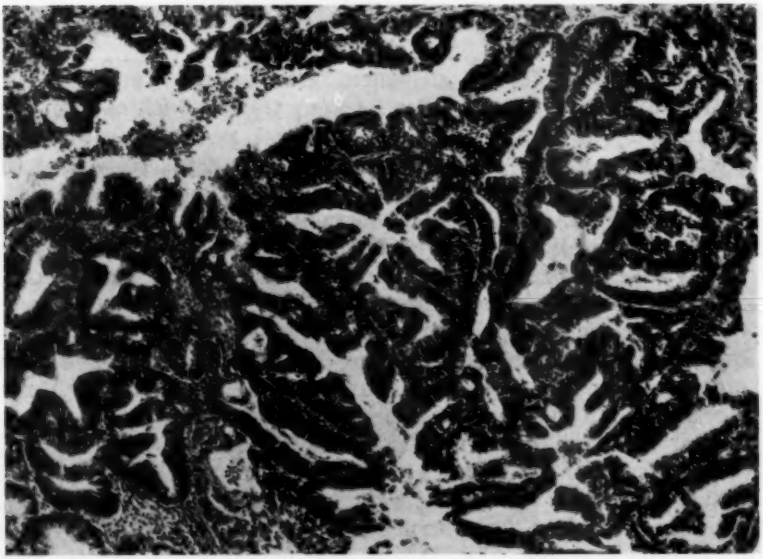

Fig. 14 — 4279/33 — Group 3, × 83.

a granulosa-cell tumour with folliculoid structures was found. She is alive and well.

Two patients (H. A. M. 14365/43 and A. B. 6263/29) were never treated with radium, although histological examination revealed a definite suspicion of malignancy; both underwent total hysterectomy and bilateral salpingo-oophorectomy at other hospitals. The histological examination of the ovarian tumour showed in the first case a granulosa-cell tumour and in the second one a malignant papilliferous cystoma. The first of these patients is alive and well, the second died 14 years after operation from heart disease, presenting no symptoms of metastases.

Although the last mentioned case has been included in the group of cases showing a granulosa-cell tumour, it is questionable whether it is possible to establish any relationship between this tumour and the endometrial changes suspicious of malignancy. Even if this possibility appears unlikely, it should be mentioned that some endometrial changes have been described as secondary to malignant ovarian tumours usually supposed to be non-functioning.

Conclusions

In the Radiumhemmet series of cancer of the uterine body, the »debatable cases» group constitutes 5.4 per cent of the total material.

Ten per cent of the 60 cases reported here, in spite of the radical treatment given, developed adenocarcinoma, five of which in the endometrium and one in the Fallopian tube.

It must be pointed out that the occurrence of these pseudo-malignant lesions in the postmenopausal period should be regarded as obviously more suspicious than at the menopause or in the reproductive period. This fact is substantiated by the finding that five of the six patients who developed a true carcinoma had passed the menopause.

As has been pointed out earlier, 24 cases showed an endometrium of a functioning type. Among these, only one case later developed unmistakeable adenocarcinoma. On the other hand, the suspicious changes were found in three of the recurrent cases in polyps, and in two in atypically hyperplastic non-functioning endometria. This finding seems to indicate that the suspicion aroused by these pseudo-malignant lesions is graver in cases showing endometrial polyps or atypical glandular proliferations in a non-functioning endometrium, than in cases with an endometrium of functioning type.

No definite conclusions can be drawn from the present study as to whether these cases should be considered to have been truly malignant ab initio.

Although it cannot be definitely stated that all the lesions would

finally have become frankly malignant, radical treatment seems justified. It must be pointed out that, since these lesions appear to be confined to the endometrium, and mainly to small portions of it, a radical effect of the treatment is to be expected.

In the writer's opinion, it is probable that if radical treatment had not been given, the number of cases which developed adenocarcinoma would have been higher.

It may be questioned whether it is as necessary to treat radically patients who exhibit atypical hyperplastic changes in a functioning endometrium but have not completed their menopause. Since these changes are not unequivocally benign, and since careful radium therapy involves little risk all patients with these changes should be given the benefit of this treatment.

Table 4

Five-year results in patients treated 1914—1941 inclusive (inclusive and exclusive of the »debatable cases»).

Total number of patients examined *inclusive of the »debatable cases»*	Alive without evidence of the disease	Absolute cure-rate *inclusive of the »debatable cases»*	Total number of patients examined *exclusive of the »debatable cases»*	Alive without evidence of the disease	Absolute cure-rate *exclusive of the »debatable cases»*	Difference in number of cases	Difference in cure rates
842	442	52.5 %	796	399	50.1 %	46	2.4 %

The difference in the rates of cure, as given in Table 4, shows the importance of making the borderline between benign and malignant epithelial lesions of the endometrium as definite as possible. In this way the comparability of the results obtained by different methods of treatment of cancer of the uterine body will be more reliable.

It appears advisable, when publishing results of treatment of cancer of the uterine body that the percentage of »debatable cases» included in the series be stated.

I wish to express my gratitude to Dr. LARS SANTESSON for his kind aid in the microscopic part of the investigation, and to Prof. JAMES HEYMAN for the constructive and stimulating criticism with which he followed my study.

SUMMARY

In this paper 60 cases with pseudo-malignant changes of the endometrial epithelium are studied from the clinical and the microscopic standpoints. All patients were treated with radium in doses commonly used for uterine cancer, and followed-up for at least 5 years. Ten per cent of the patients later developed adenocarcinoma. Through the histological investigation evidence is given of the importance of drawing a borderline as definite as possible between benign and malignant lesions, in order to justify the inclusion or the exclusion of the »debatable cases» in the statistics of cancer of the uterine body.

ZUSAMMENFASSUNG

In dieser Arbeit werden 60 Fälle von pseudo-malignen Veränderungen des Epithels des Endometriums von klinischen und mikroskopischen Gesichtspunkten aus studiert. Sämtliche Patientinnen wurden mit den bei Gebärmutterkrebs gebräuchlichen Dosen von Radium behandelt und mindestens 5 Jahre lang verfolgt. Bei 10 % der Kranken kam später ein Adenokarzinom zur Entwicklung. Durch die histologische Untersuchung wird die Bedeutung der Ziehung einer möglichst scharfen Grenzlinie zwischen gutartigen und bösartigen Veränderungen bewiesen, um die Mitaufnahme oder die Ausschliessung »zweifelhafter Fälle» bei der Aufstellung von Statistiken über Krebs des Corpus uteri zu rechtfertigen.

RÉSUMÉ

Dans cet article l'auteur étudie au point de vue clinique et anatomo-pathologique 60 cas d'altérations pseudo-malignes de l'épithelium du corps uterin. Toutes les patientes ont été traitées par les doses de radium habituellement appliquées au cancer uterin et chaque patiente suivie pendant cinq ans au minimum. Dix pour cent développèrent en suite un adenocarcinome. L'examen anatomo-pathologique montre l'importance qu'il y a à distinguer avec le plus de précision possible entre les lesions benignes et les lesions malignes, afin de justifier l'inclusion ou l'exclusion de cas »douteux» dans les statistiques du cancer du corps uterin.

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FROM THE I. ROENTGENDIAGNOSTIC DEPARTMENT OF SÖDERSJUKHUSET, STOCKHOLM, SWEDEN (CHIEF: DOCENT G. JÖNSSON)

ROENTGEN EXAMINATION OF THE SUBTALOID JOINT IN FRACTURES OF THE CALCANEUS[1]

by

Bror Brodén

Many cases of comminuted fracture of the calcaneus disclose joint involvement with damage to the posterior articular surface of the calcaneus. A lateral fragment with the outer part of the articular facet is displaced and tilted. Nowadays fractures of this kind are often subjected to operation. The displaced fragment is reduced and the underlying cavity is filled with bone chips.

The projections generally employed at roentgen examination of the calcaneus, viz. the lateral and semi-axial views, offer inadequate information regarding the appearance of the posterior articular surface of the calcaneus. This surface should be examined by means of projections clearly reproducing the subtaloid joint.

The posterior articular surface of the calcaneus has a shape that may be compared to a part of the curved surface of a frustum of a cone, with the base directed lateroposteriorly and the top medioanteriorly. The angle between the central axis of the cone and the longitudinal axis of the foot equals approximately 45° (Fig. 1). The inclination of the joint surface is slightly medioanterior, the angle being about 15°. The tangents to the anterior and posterior parts of the joint

Fig. 1.

[1] Submitted for publication, Dec. 29, 1948.

Fig. 2.

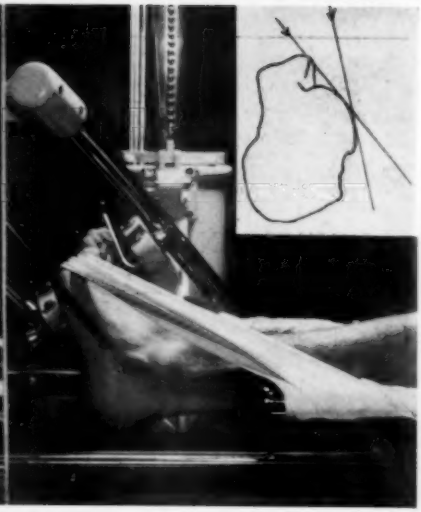

Fig. 3.

Fig. 4.

Fig. 5.

Figs. 2—5: Projection I

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

Figs. 6—9: Projection II

Fig. 10. Lateral view.

Fig. 11. Semi-axial view.

Calcaneus fracture.

400 Fig. 12. 300 Fig. 13. 100 Fig. 14.

Fig. 15.

Figs. 12—14. Same case as in Figs. 10 and 11. Projection I. Fracture involving the subtaloid joint. The posterior articular surface of the calcaneus is damaged. A lateral fragment is displaced.

Fig. 15. Same case. Projection II.

400 Fig. 16. 330 Fig. 17. 200 Fig. 18.

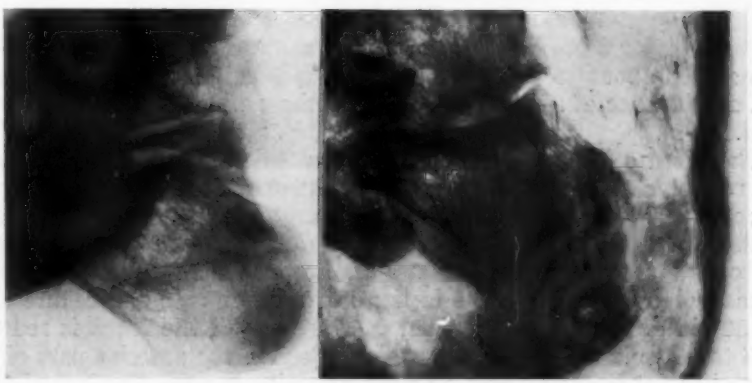

Fig. 19. Fig. 20.

Figs. 16—18. Calcaneus fracture with joint involvement, of on the whole the same type as in Figs. 12—15.

Fig. 19. Same case as in Figs. 16—18. Projection II: No part of the posterior articular surface of the calcaneus is congruent with the corresponding articular surface of the talus.

Fig. 20. Calcaneus fracture, operated and plastered. The subtaloid joint is clearly visible through the plaster.

surface, drawn in a plane perpendicular to the central axis of the cone, intersect at an angle of approximately 30° (see drawing in Fig. 3).

The corresponding articular surface of the talus is congruent to that of the calcaneus.

It emerges from the above account of the anatomy of the talocalcanean joint that, in principle, a roentgen examination of this joint is best performed at projections in two planes perpendicular to one another at an angle of 45° to the longitudinal axis of the foot. This can be carried out in the following way.

Projection I: The patient supine. Leg and foot are turned 45° inwards with right angle flexion at the ankle joint. The central ray is directed against a point 2—3 cm caudoventrally to the lateral malleolus. Four pictures are taken with the tube angled 40, 30, 20 and 10°, respectively, towards the head (Figs. 2—5).

The picture taken with the tube angled 40° shows the anterior part of the talocalcanean joint, the picture with the tube angled 10° reproducing the posterior part. Some of the pictures (generally those with the tube angled 30 or 20°), make the articulation between the sustentaculum and the talus visible.

Projection II: The patient supine. Leg and foot are turned 45° outwards with right angle flexion at the ankle joint. The central ray is directed against a point 2 cm caudoanteriorly to the medial malleolus with the tube angled about 15° towards the head. It is suitable to take 3 pictures with a difference of 3—4 degrees. One of these will, as a rule, be perfect (Figs. 6—9).

The picture in projection I, which was taken with the tube angled 40°, resembles the projection used by HUSFELDT and HANSEN and recommended by ANTHONSEN in 1943, in an article in this journal. ANTHONSEN writes: »The foot is placed in dorsal flexion with its lateral side towards the film. The central ray is directed against a point just below the malleolus medialis with an inclination of 25° in craniodistal direction, and 30° in dorsoventral direction, the distance of the focus is reduced to 25 to 35 cm.» — By means of this projection the anterior part of the subtaloid joint is reproduced. The ray direction is more transversal than is the case described in projection I.

Projection II, which has been described by HALLGRÍMSSON and used by him in an examination of the height of the articular cartilage, has also proved of great value when studying a calcaneus fracture with joint involvement. The dorsoplantar compression can be examined in pictures taken at this projection. The sinus tarsi is distinctly visible.

Sometimes the talocalcanean joint can be seen in an ordinary semiaxial view of the calcaneus, though only in cases where the foot can be bent backwards. Dorsiflexion is, as a rule, impossible to perform owing to the painfulness of the fracture. In the projections described here no dorsiflexion of the foot is required. These projections can also be applied at moderate plantar flexion at the ankle joint — with the tube more angled towards the head. At projection I, the ray direction will often

pass in the same plane as the oblique fracture involving the joint thus clearly visualized (Figs. 12—14 and 16—18).

The roentgenograms published in this article have been taken on the Lysholm skull table. Intensifying screens have been used. Exposure factors: 65 kVp. 80—100 mA secs.

SUMMARY

The author draws attention to two projections suitable for examination of the subtaloid joint in calcaneus fractures.

ZUSAMMENFASSUNG

Verf. macht auf zwei Projektionen aufmerksam, die sich zur Untersuchung des unteren Sprunggelenks bei Calcaneusfrakturen eignen.

RÉSUMÉ

L'auteur attire l'attention sur deux projections convenant à l'examen de l'articulation sous-astragalienne dans les fractures du calcanéum.

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FROM THE ROENTGEN DIAGNOSTIC DEPARTMENT OF KAROLINSKA SJUKHUSET, STOCKHOLM, SWEDEN (HEAD: PROFESSOR ÅKE ÅKERLUND)

»OVERSHOT AXIAL PROJECTION«

ITS VALUE IN THE ROENTGEN EXAMINATION OF THE ACCESSORY SINUSES[1]

by

Sölve Welin

Since the frontal sinuses are the most difficult to examine clinically, the roentgen examination is all the more important from the diagnostic point of view. In practice, however, radiographs of these sinuses may be difficult to interpret, and in consequence pathological conditions in the frontal sinuses are often hard to evaluate.

In order to improve radiological diagnostic in this field we therefore introduced six years ago a new projection — the so-called overshot axial projection. As a result of the consistent use of this projection during this period we have found that the reliability of the roentgen findings has in many cases been increased from the surgical point of view.

In this so-called overshot axial projection — of which a description has earlier been given in the British Journal of Radiology (1948) — the patient may be in a sitting or supine position with the beam directed submento-vertically. The head is extended backwards so that the mandible is projected in front of the frontal sinuses and the beam is tangential to their posterior walls (fig. 1 a).

In this projection (fig. 1 b) the antero-posterior depth of the frontal sinuses can be clearly estimated both in their medial plane and their lateral extensions. Furthermore, the thickness of their walls can be evaluated, which is of great importance in the analysis of these pictures.

The varying degrees of translucency in the different parts of the frontal sinuses in the postero-anterior projection may sometimes be so marked as to simulate a pathological density and lead to an erroneous conclusion. This difference in translucency can at times depend on a different depth of the air volume in one sinus as compared with the other, and abnormal bulges can give a similar difference in the same paranasal sinus. The latter condition is illustrated by the following case.

[1] Submitted for publication, Jan. 8, 1949.

Fig. 1 a. Diagram of the projection.

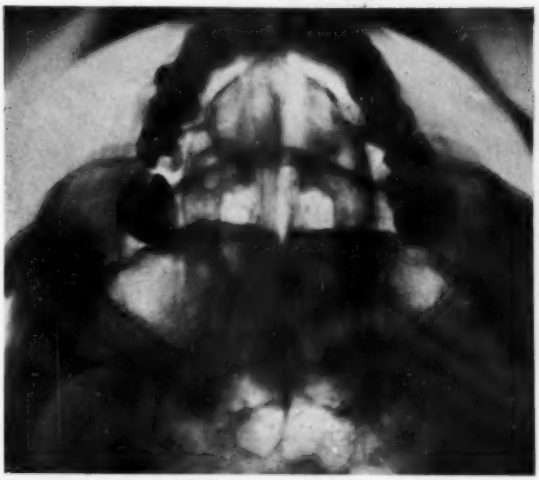

Fig. 1 b. Radiograph in the projection.

Case No. 1403/43, a soldier, aged 20 years. For one month he had suffered from severe pain in the left frontal region. Since at the same time he had persistent rhinitis on the left side and radiological examination at another hospital had revealed a density over the medial part of the left frontal sinus, the patient was sent to the Ear, Nose and Throat Department of Karolinska Sjukhuset with the diagnosis of left frontal sinusitis. Our radiological examination also appeared to show a density over the medial parts of both frontal sinuses as well as over the left ethmoids (fig. 2). The overshot axial projection nevertheless showed that this decreased translucency in the frontal sinuses was caused by osteoma-like formations on their anterior walls. It was thus possible in this case by means of the overshot axial projection to exclude an affection of the frontal sinuses and thus to prevent an unnecessary surgical intervention.

The affection of the left ethmoids revealed radiologically was thus sufficient in this case to explain entirely the patient's symptoms of which there was subsequently complete remission following conservative treatment.

Different degrees of thickening or irregular sclerosis of the walls of the frontal sinuses can also simulate an opaque or absent sinus, as is illustrated by the following case.

Case No. 3247/45, a man, aged 66 years. Six months after an operation on the left maxillary sinus (Caldwell-Luc operation) there was increasing tenderness on pressure over the left cheek. There was also a protrusion of the left eyeball and lacrimation on the left side. No rhinitis, fever, nor pain.

Judging by the roentgen pictures with a postero-anterior direction of the beam, it was very doubtful whether there was any frontal sinus on the left side (fig. 3 a). The bone structure was entirely homogeneous and almost as dense as normal compact bone. On the lateral picture (fig. 3 b) it was, however, possible in the medial plane to distinguish a frontal sinus which was considerably narrowed and whose anterior wall was of consider-

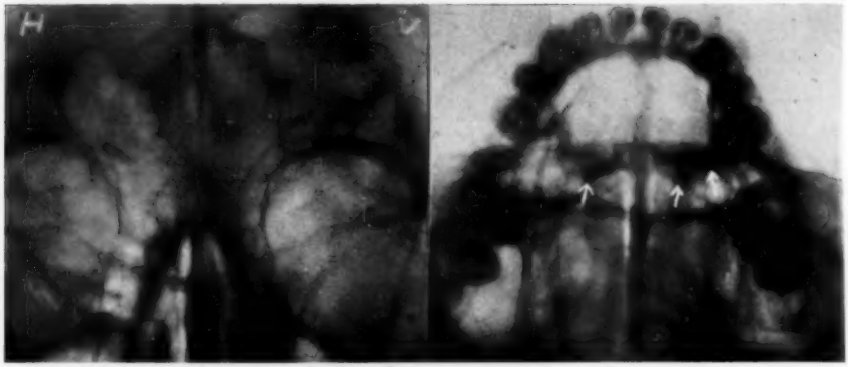

Fig. 2 a. Fig. 2 b.

Fig. 2. The left radiograph shows an apparent pathological opacity of the medial parts of the frontal sinuses and of the left ethmoids. The right shows that the opacity in the frontal sinuses is due to a thick anterior wall (osteoma) and also confirms the ethmoiditis.

able thickness. On the overshot axial projection picture (fig. 3 c) the frontal sinuses appeared very distinctly, and a definite impression was obtained of the thickness of their walls. It could also be seen that the frontal bone laterally of the left frontal sinus was somewhat more than one centimetre thick. Since the subraorbital margin and the anterior part of the roof of the orbit felt thicker than usual clinically and even bulged downwards into the orbit, it was necessary in addition to an inflammatory process also to envisage the possibility of an osteofibroma of considerable maturity. Owing to the density on the left side shown on the overshot axial projection picture, the diagnosis of sinusitis was made. The considerable thickness of the anterior wall of the frontal sinus and — to a lesser degree — also of the posterior wall was considered to depend on an unusually pronounced sclerosis on an inflammatory basis. This was also verified at operation.

Operation (15. 12. 1945): Left frontal sinus operation was performed according to Barány's method. Beneath a cortex approximately 5 mm thick a fairly large frontal sinus was found with a grayish-red extremely swollen mucous membrane. The sinus was almost entirely filled with thick, greenish-yellow pus.

In this case with its pronounced unilateral osteosclerosis resulting from and old inflammatory process with much bony proliferation, our first standard projection with the beam directed horizontally (postero-anterior) towards the middle of the nose could thus have led to the opinion that one of the frontal sinuses was lacking. Through the use of the »overshot axial picture» it was possible to determine whether this was true or only apparent. The view using the postero-anterior beam and the »overshot axial picture» are thus complementary and the projection is thus superior to the ordinary profile picture when the depth of the frontal sinuses in their entire extent is to be established.

Despite the great improvement brought about by the introduction

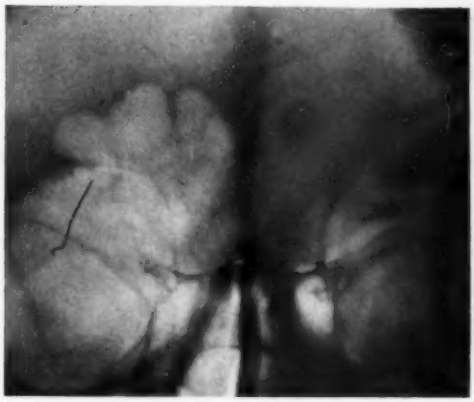

Fig. 3 a.

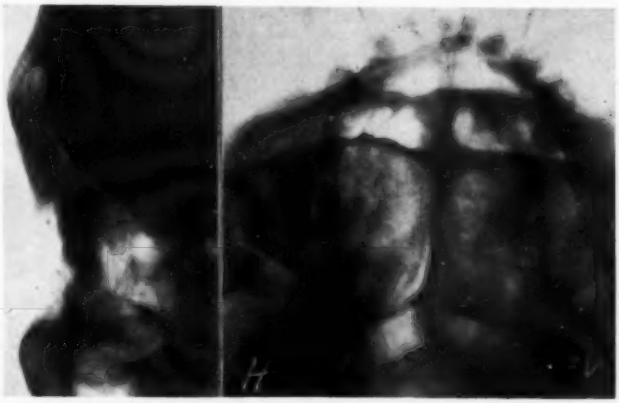

Fig. 3 b. Fig. 3 c.

Fig. 3. a. The radiograph with postero-anterior direction of the beam shows an apparent absence of the left frontal sinus.
Fig. 3 b. Lateral picture. The frontal sinus is present and narrowed. The anterior wall of considerable thickness.
Fig. 3 c. The overshot axial projection shows the depth of the sinus and that there is osteosclerosis of the anterior wall.

of this new projection, cases are nevertheless still found in which it is impossible to establish definitely by means of radiological examination whether a frontal sinus is affected or not. Figs. 4 a and b illustrate such a case. It can immediately be seen from the pictures that the left maxillary

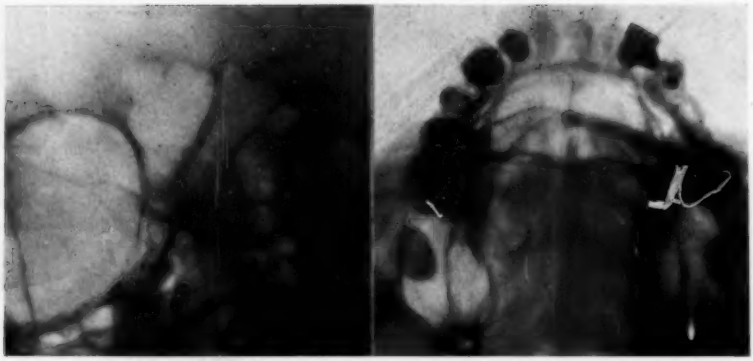

Fig. 4 a. Fig. 4 b.

Fig. 4. The left radiograph shows a density over the left frontal sinus, the left ethmoids and the left maxillary sinus. The overshot axial projection shows greater thickness of the bony walls in the left frontal sinus and lesser depth which perhaps is enough to explain the decreased translucency.

sinus and the left ethmoids are affected. Foul-smelling pus was also found on puncture of the maxillary sinus. It is not possible to state definitely whether the great difference in translucency between the right and left frontal sinuses is due to an opacity of the left frontal sinus on an inflammatory basis or whether it can be explained by the greater thickness of the bony walls in the left frontal sinus and its lesser depth. Such cases are nevertheless fairly uncommon and they will obviously become still more uncommon with increased experience.

SUMMARY

The writer describes the technique in so-called overshot axial projection and states the reasons for its use in the examination of the accessory sinuses.

ZUSAMMENFASSUNG

Verf. beschreibt die Technik bei sog. »overshot axial projection» und stellt die Gründe i hrer Verwendung bei der Untersuchung der akzessorischen Sinusse fest.

RÉSUMÉ

L'auteur décrit la technique de la projection axiale dite »en dessus» et donne les raisons de son emploi dans l'examen des sinus accessoires.

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